Delivering the Future of Genomic Medicines

March 13, 2024

Forward-Looking Statements

This presentation, and accompanying oral commentary, contains forward-looking statements regarding our current expectations. These forward-looking statements include, without limitation, statements relating to: the therapeutic and commercial potential of our product candidates and engineered capsids, including the ability of STAC-BBB to unlock significant potential for the treatment of various neurological diseases, our plans to focus on epigenetic regulation and capsid engineering, the potential to develop, obtain regulatory approvals for and commercialize durable, safe and effective therapies to treat certain diseases and the timing, availability and costs of such therapies, the potential to use ZF, ZF-TR, SIFTER and other technologies to develop durable, safe and effective therapies and capsids, the potential for us to benefit and earn milestone and royalty payments from our collaborations and the timing of any such benefits and payments, plans and expectations to seek partners or collaborators for certain of our programs regarding our financial resources, including the sufficiency thereof and plans to reduce our operating expenses, the impact of our streamlined structure and future potential cost reductions, anticipated plans and timelines for us and our collaborators dosing patients in and conducting our ongoing and potential future clinical trials and presenting data from our clinical trials and making regulatory submissions, the anticipated advancement of our product candidates to late-stage development, including potential future registrational trials, execution of our corporate strategy, our pipeline, the identification of additional targets, and the advancement of preclinical programs to the clinic, key milestones and catalysts, and other statements that are not historical fact. These statements are not guarantees of future performance and are subject to certain risks and uncertainties that are difficult to predict. Our actual results may differ materially and adversely from those expressed. Factors that could cause actual results to differ include, without limitation, the uncertain and costly research and development process, including the risk that preclinical results may not be indicative of any future clinical trials, risks and uncertainties related to macroeconomic factors, including as a result of ongoing overseas conflicts, disruptions in access to bank deposits and lending commitments due to bank failure, on the global business environment, healthcare systems and business and operations of us and our collaborators, including the initiation and operation of clinical trials; the research and development process; the uncertain timing and unpredictable results of clinical trials, including whether preliminary or initial clinical trial data will be representative of final clinical trial data and whether final clinical trial data will validate the safety, efficacy and durability of product candidates; the impacts of clinical trial delays, pauses and holds on clinical trial timelines and commercialization of product candidates; the unpredictable regulatory approval process for product candidates across multiple regulatory authorities; the manufacturing of products, product candidates and capsids; the commercialization of approved products; the potential for technological developments that obviate technologies used by us and our collaborators; the potential for us or our collaborators to breach or terminate collaboration agreements; the potential for us to fail to realize our expected benefits of our collaborations; the uncertainty of our future capital requirements, financial performance and results, our lack of capital resources to fully develop, obtain regulatory approval for and commercialize our product candidates, including our ability to secure collaboration for some of our programs, our ability to secure the funding required to advance our preclinical programs and/or initiate a potential registrational trial of isaralgagene civaparvovec in a timely manner or at all; and our need for substantial additional funding to execute our operating plan and to operate as a going concern, including the risk we will be unable to obtain the funding necessary to advance our preclinical and clinical programs and to otherwise operate as a going concern in which case we may be required to cease operations entirely, liquidate all or portion of our assets and/or seek protection under applicable bankruptcy laws middle all or a portion of out. There can be no assurance that we and our collaborators will be able to develop commercially viable products. These risks and uncertainties are described more fully in our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, as filed with the Securities and Exchange Commission (“SEC”) and future reports filed with the SEC. Forward-looking statements contained in this presentation speak only as of the date hereof, and we undertake no duty to update such information except as required under applicable law. This presentation concerns investigational product candidates that are under preclinical and/or clinical investigation, and which have not yet been approved for marketing by any regulatory agency. They are currently limited to investigational use, and no representations are made as to their safety or efficacy for the purposes for which they are being investigated. Any discussions of safety or efficacy are only in reference to the specific results presented here and may not be indicative of an ultimate finding of safety or efficacy by regulatory agencies.

Sangamo is a differentiated genomic medicine company focused on treating debilitating neurological diseases

Sangamo THERAPEUTICS

Potent zinc finger epigenetic regulation technology, with neurology programs advancing towards the clinic

Industry-leading AAV capsid discovery platform enabling non-invasive intrathecal and intravenous delivery to the brain

Powerful research platform **continually innovates in new modes of genome modulation** to support value creation for both wholly owned programs and potential partners

SHARP STRATEGIC FOCUS IN NEUROLOGY

Track record of successful partnerships, with $220m in potential near-term milestones from Pfizer (Hem A BLA submission expected early 2025). **Seeking partner for Fabry program, with clear pathway to potential registration.**

OPTIMIZING ASSET VALUE

Why neurology genomic medicines?

- Widespread, debilitating diseases, largely unserved by current approaches
- Many neurology indications are single-gene or gene-associated
- Genomic medicines are well suited to neurology:
  - Targeting diseases at the DNA level reduces therapeutic complexity
  - Gene expression can be fine-tuned to the level needed for proper brain function
  - Potential for durable effect as most brain cells do not divide
- Addressing the issues of widespread brain delivery is critical to creating an effective neurology medicine

Sangamo THERAPEUTICS

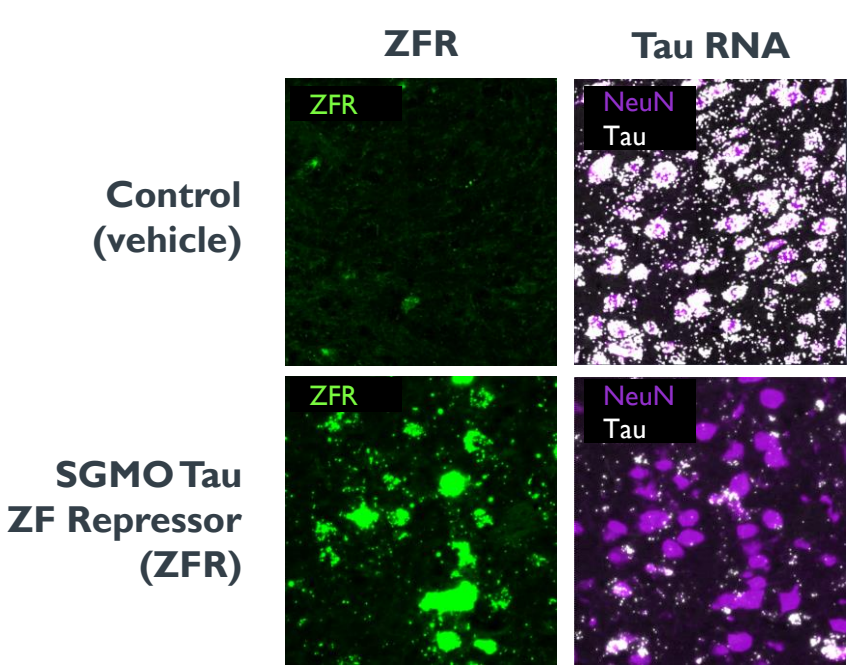
Sangamo is the only biopharma with both the wholly owned epigenetic regulation *and* capsid delivery capabilities needed to create neurology genomic medicines

Genome-Targeting Cargo

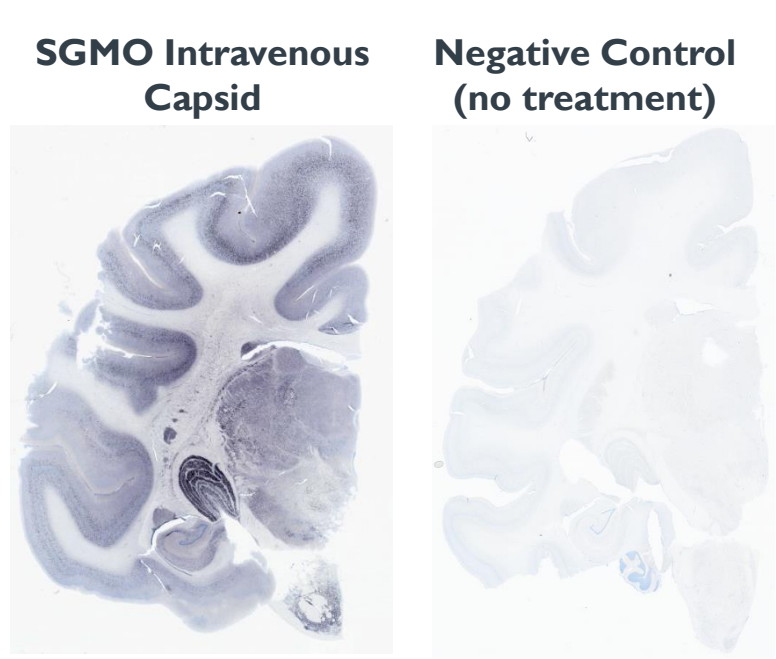
Epigenetic regulation platform

Capsid Delivery Engine

AAV capsid delivery platform via intravenous delivery



Non-human primate brainstem



Non-human primate

Future of Neurology Genomic Medicines

Sangamo's neurology pipeline provides opportunities for wholly owned program advancement and potential partnering opportunities

WHOLLY OWNED PRIORITY PROGRAMS	**Chronic Neuropathic Pain** Nav1.7	**Prion Disease** PRNP	**Tauopathies (AD, PSP, FTD)** MAPT			
CURRENTLY PAUSED: UNLOCKED BY INTRAVENOUS CAPSID	**Parkinson's Disease** SNCA	**Phelan-McDermid Syndrome** SHANK3	**Myotonic Dystrophy Type I** DMPK	**Dravet Syndrome** SCN1A	**Haploin-sufficiency Syndrome** SCN2A	
PARTNERED PROGRAMS	**Amyotrophic Lateral Sclerosis (ALS)** C9orf72 ALEXION AstraZeneca Rare Disease	**Huntington's Disease** HTT Takeda				

Cerebrospinal fluid (CSF) capsid

Intravenous (IV) capsid

AD: Alzheimer's disease; PSP: Progressive supranuclear palsy; FTD: Frontotemporal dementia;

Gateway indications unlock broader neurology pipeline

- ✓ Targets validated by human genetics
- ✓ Well-defined patient populations
- ✓ Delivery achievable with AAV
- ✓ Quantifiable patient outcomes on a rapid timeline

Chronic Neuropathic Pain (Nav1.7)

Est. 43,000+ Patients in US**

- Significant unmet medical need
- Highly specific repression, with no impact to other Nav channels
- Starting with small fiber neuralgia. Potential to broaden to other indications.
- Potentially rapid development pathway given short timescale to clinical efficacy readout
- IND submission expected 4Q 2024*

Prion Disease

Est. 1,500+ Patients Per Year***

- Devastating condition. Rapidly progressive and always fatal.
- Highly potent repression of prion in mice brains, significantly extending survival in a disease mouse model
- Potential for accelerated regulatory and commercialization pathway
- CTA-enabling studies are in progress, CTA submission expected 4Q 2025*

** Subject to our ability to secure adequate funding*
***With Small Fiber Neuralgia*
****US (per CDC) and Europe (https://www.eurocjd.ed.ac.uk/)*

Sangamo THERAPEUTICS

Company pipeline and business development opportunities

CORE NEUROLOGY PIPELINE

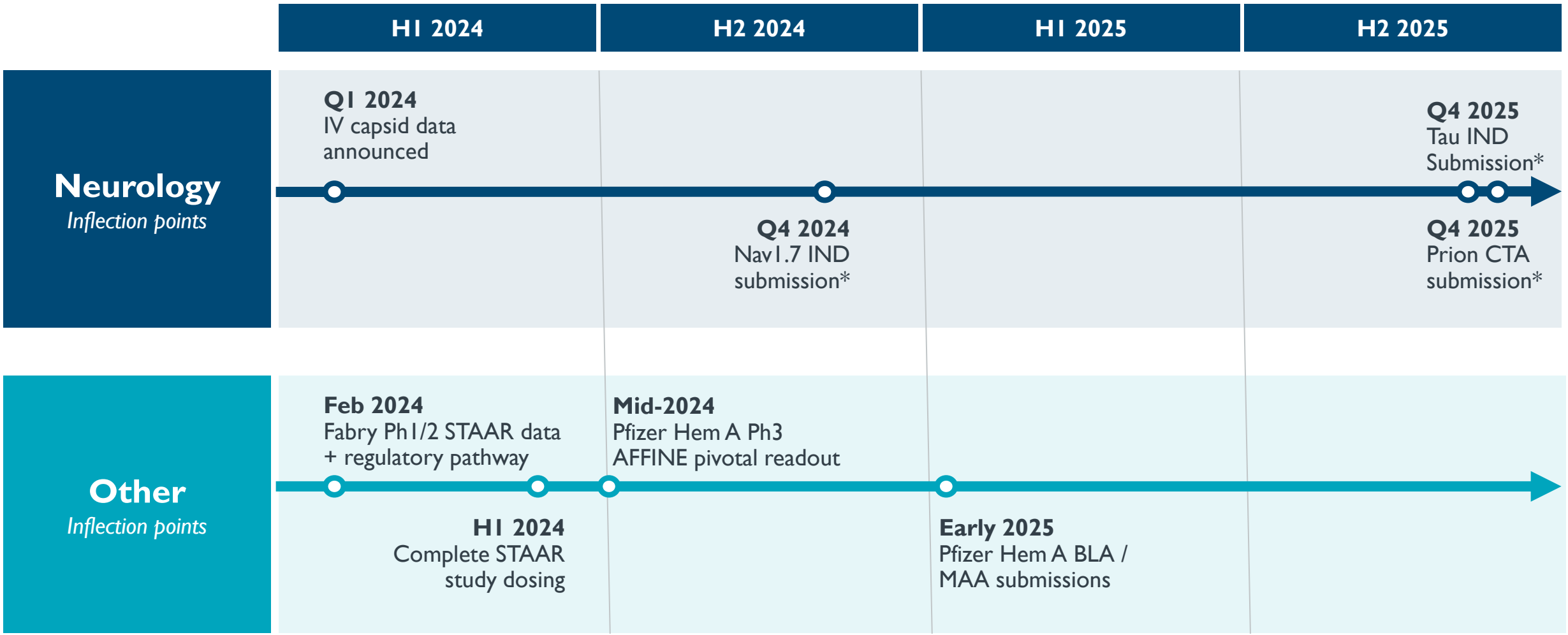
Indication	Preclinical	Phase 1/2	Pivotal	Partner	Anticipated Milestones*
Chronic Neuropathic Pain *(Nav1.7)*	*Data presented at ASGCT 2023*			-	**Q4 24:** Nav1.7 IND submission
Prion Disease	*Data presented at Prion 2023*			-	**Q4 25:** Prion CTA submission
Tauopathies				-	**As early as Q4 25:** Tau IND submission
ALS/FTD				ALEXION AstraZeneca Rare Disease	
Huntington's Disease				Takeda	

OTHER PROGRAMS

Indication	Preclinical	Phase 1/2	Pivotal	Partner	Anticipated Milestones
Hemophilia A (Giroctogene fitelparvovec)	*Data presented at ASH 2023*			Pfizer	**Mid-2024:** Phase 3 AFFINE trial pivotal readout **Early 2025:** BLA and MAA submissions
Fabry Disease (Isaralgagene civaparvovec)	*Data presented at WORLDSymposium 2024*			-	**1H24:** Phase 1/2 STAAR study dosing completion
Renal Transplant *(TX200)*	*Six patients dosed in Phase 1/2*			-	**1H24:** Phase 1/2 STEADFAST study dosing completion
Oncology				Kite A GILEAD Company	Collaboration agreement expires April 2024

** Subject to our ability to secure adequate funding*

Anticipated near-term milestones



** Subject to our ability to secure adequate funding*

Multiple biopharma collaborations demonstrate our platform's potential and have provided significant economics for Sangamo

Gene Therapy

Pfizer

Cell Therapy

Kite, A GILEAD Company

Genome Engineering

ALEXION, AstraZeneca Rare Disease

Takeda

Prevail Therapeutics, A Wholly Owned Subsidiary of Eli Lilly and Company

CHROMA MEDICINE

$817m
cash received from partners to date

Up to $1.9b
in potential future milestones and exercise fees assuming exercise of all options and targets

Additional potential product royalties

Numerous Benefits of Partnerships:

Large Pharma buy-in validates the science

Provides potential non-dilutive capital to advance pipeline

Leverages partner domain expertise

Promotes optimal resource allocation to advance late-stage clinical development

Company Highlights

Advancing epigenetic regulation cargo and novel AAV capsids for high-value gateway neurology diseases like chronic neuropathic pain and prion disease

Proprietary AAV blood-brain barrier penetrant capsid (STAC-BBB) with industry leading CNS tropism in non-human primates

STAC-BBB potentially unlocks multiple neurology epigenetic programs that could be advanced ourselves or with partners

Prion disease program has the potential to rapidly validate STAC-BBB in humans

Pfizer collaboration in Hem A brings revenue-bearing opportunity – $220m potential milestones and 14-20% potential sales royalties, if approved

Fabry program generating compelling Phase 1/2 clinical data. Ready for registrational study, with abbreviated clinical pathway aligned with U.S. FDA. Seeking potential partner.

4Q23 Business Updates

4Q23 Key Takeaways

Announced new industry-leading neurotropic AAV delivery capsid

Data from new novel proprietary neurotropic adeno-associated virus (AAV) delivery capsid, STAC-BBB, demonstrated industry-leading blood-brain barrier (BBB) penetration in non-human primates (NHPs), with capsid-enabled delivery of zinc-finger payloads targeting prion disease and tauopathies resulting in potent and widespread repression of target genes.

Chronic neuropathic pain and prion disease preclinical programs advance, with investigational new drug (IND) and clinical trial authorization (CTA) submissions expected in the fourth quarters of 2024 and 2025, respectively*.

Fabry Disease

- Announced U.S. Food and Drug Administration (FDA) alignment on an abbreviated pathway to potential approval, grant by European Medicines Agency (EMA) of priority medicines (PRIME) eligibility and Innovative Licensing and Access Pathway (ILAP) by UK Medicines and Healthcare products Regulatory Agency (MHRA) in Fabry disease.
- In active discussions with potential Fabry collaboration partners.

Hem A (Pfizer)

- Phase 3 AFFINE pivotal readout expected in mid-2024.
- Pfizer anticipates BLA and MAA submissions by early 2025 if the pivotal readout is supportive.

** Subject to our ability to secure adequate funding*

Financial Highlights

- Approximately **$81 million in cash, cash equivalents, and marketable securities** as of December 31, 2023 which, in combination with potential cost reductions, will be sufficient to fund planned operations into 3Q 2024, excluding any additional capital raised.
- We are actively pursuing opportunities to raise additional capital.
- We have proactively reduced our Non-GAAP operating expenses by ~50% year-over-year as we transition into a focused neurology company in 2024.

Sangamo THERAPEUTICS

Q4 Pipeline Progress & Anticipated Milestones

NEUROLOGY EPIGENETIC REGULATION

- ✓ Announced data from novel proprietary neurotropic AAV capsid (STAC-BBB) demonstrating industry-leading blood-brain barrier penetration and brain transduction in non-human primates.
- ✓ Advanced IND-enabling activities for Nav1.7 for chronic neuropathic pain and CTA-enabling activities for Prion.
- ✓ Resumed development of tau program, leveraging the STAC-BBB capsid.
- • IND submission for Nav1.7 expected in Q4 2024*.
- • CTA submission for Prion expected Q4 2025*. IND submission for tau could occur as early as Q4 2025*.

HEMOPHILIA A (PFIZER)

- ✓ Updated Phase 1/2 ALTA data presentation at ASH, December 11, 2023.
- • Pivotal data read-out expected in mid-2024.
- • BLA and MAA submissions anticipated in second half of 2024 if pivotal data readout is supportive.

FABRY DISEASE

- ✓ Dosed an additional seven patients in Phase 1/2 STAAR study to achieve a total of 32 patients dosed.
- ✓ Updated STAAR data presented at WORLD*Symposium* showing sustained benefit and differentiated safety profile.
- ✓ Aligned with FDA that data from a single, adequate, and well-controlled study may form the primary basis of approval, enabling a potentially abbreviated and more cost-effective pathway to BLA submission than originally anticipated.
- ✓ Granted PRIME medicine eligibility from the EMA and ILAP from UK MHRA.
- ✓ Completed screening and enrollment in the Phase 1/2 STAAR study.
- • Expect to complete dosing of the remaining enrolled patients in the first half of 2024.

CAR TREG IMMUNE REGULATION

- ✓ Dosed two additional patients in the Phase 1/2 STEADFAST study, including first patient in the new fourth, highest dose cohort.
- ✓ In alignment with previously announced strategic transformation, announced winddown of the Company's French research and manufacturing operations and a corresponding reduction in workforce.
- • Expect to dose up to two additional patients in the fourth highest-dose level cohort by the end of Q2 2024.
- • Continue to seek a potential collaboration partner or external investment in the CAR-Treg cell therapy programs.

** Subject to our ability to secure adequate funding*

We have focused resources and reduced OpEx by ~50% year-on-year. We expect to reduce Non-GAAP OpEx to under $105M in 2025 as we transition our legacy programs.

Historical

$817m
Cash Received from Partners to date

$252.7m*
Non-GAAP OpEx – FY 2023

~$81.0m
Cash and Marketable Securities Balance as of 12/31/23

Forward Looking

Up to $1.9b
In potential future milestones and exercise fees, assuming exercise of all options and targets

Up to $220m
in potential milestone payments from Hemophilia A†, plus 14-20% in potential sales royalties

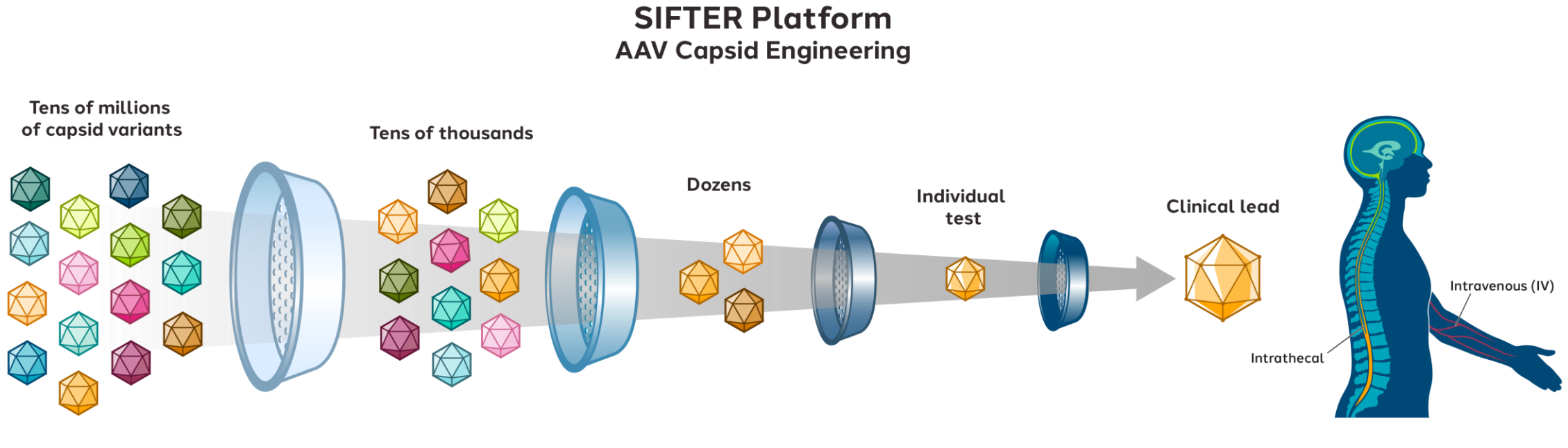
$125 – $145m** *(2024)*
Reiterated Non-GAAP OpEx Guidance excludes certain non-cash charges as noted below***

** On a GAAP basis, the 2023 operating expenses were $450.2 million which included impairment of goodwill of $38.1 million, impairment of indefinite-lived intangible assets of $51.4 million, impairment of long-lived assets of $65.5 million, depreciation and amortization of $15.1 million and stock-based compensation expense of $27.4 million.*
*** Assuming additional funding.*
**** On a GAAP basis we expect our 2024 operating expenses to be in the range of $145 - $165 million, including anticipated depreciation and amortization of $7 million and stock-based compensation expense of $13 million.*
† Currently in Phase 3 trial with Pfizer

Sangamo THERAPEUTICS

Achieving Widespread Central Nervous System Delivery for Optimal Therapeutic Benefit

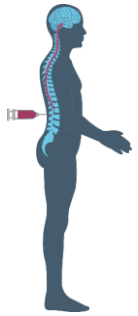
Widespread central nervous (CNS) delivery is challenging with conventional AAVs. Our SIFTER platform enables selection of neurotropic AAV capsids to advance our innovative preclinical programs to the clinic.



SIFTER: *Selecting In vivo For Transduction and Expression of RNA*

The Sangamo SIFTER platform is delivering high value neurotropic AAV capsids

Engineered capsids for cerebrospinal fluid delivery



Lead capsids characterized in non-human primates

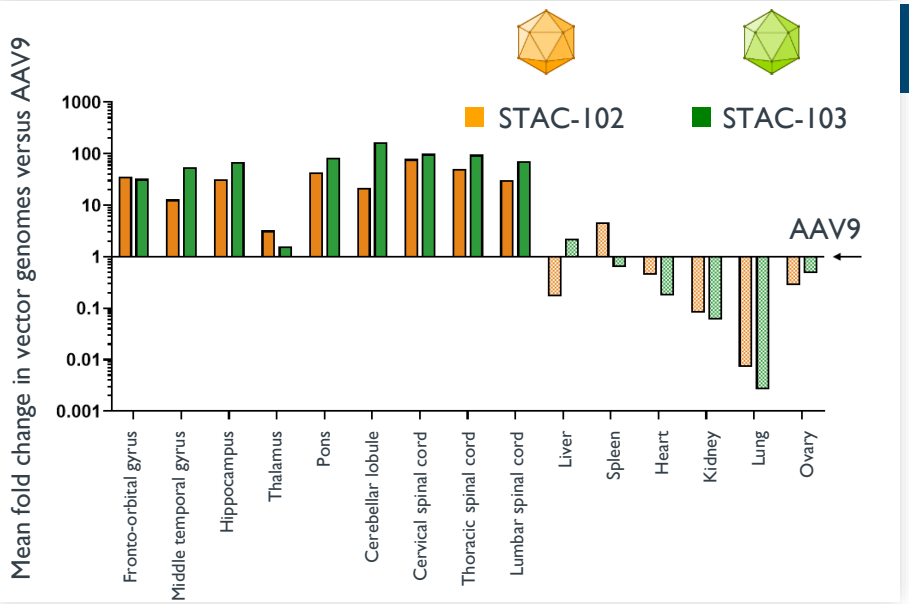
10-100x higher neuronal transgene expression compared to AAV9

Demonstrated on-target pharmacology with minimal safety signal

10-100x higher CNS vector genome delivery than AAV9 and decreased peripheral distribution

Prevail THERAPEUTICS — A Wholly Owned Subsidiary of Eli Lilly and Company

Subject of a research evaluation and option agreement with Prevail Therapeutics (Eli Lilly)



Engineered capsids for intravenous delivery

STAC = **S**angamo **T**herapeutics **A**AV **C**apsid

Lead capsid robustly penetrates the blood-brain-barrier, with enhanced CNS-tropism in non-human primates

Industry-leading brain barrier penetrant capsid (STAC-BBB) → 700-fold better enrichment than the benchmark AAV9 → Widespread brain distribution with de-targeting of other tissues, e.g., dorsal root ganglia (DRG) and liver → Capsid-enabled delivery of zinc-finger payloads targeting prion disease and tauopathies resulted in potent repression of target genes

Key characteristics of a blood-brain barrier (BBB) penetrant capsid

- Broad brain coverage
- Enhanced enrichment in the brain compared to other published capsids
- Widespread neuronal transduction
- Neuronal transduction in key brain regions integral to disease pathology
- Consistency in results across animal subjects
- Clear dose response curve for ZF expression
- Clear dose response curve of target reduction
- De-targeting of the liver, dorsal root ganglia and other organs
- Easily manufacturable at scale

Brain regions *and associated disease*

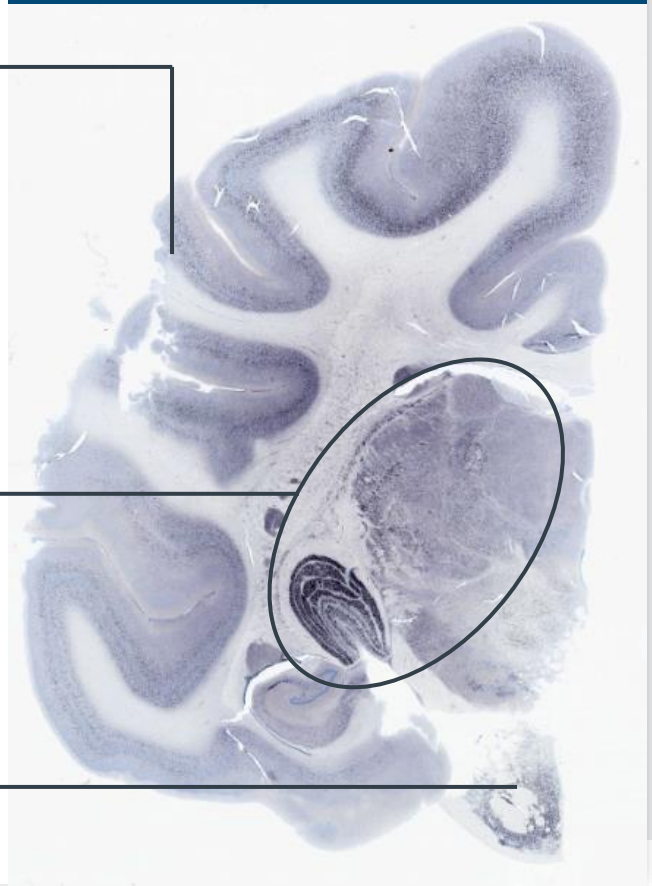
Cortical regions (e.g. postcentral gyrus)
Alzheimer's disease
Parkinson's disease
ALS, Dravet syndrome

Thalamic regions (e.g. LGN, thalamus)
Prion disease
Alzheimer's disease

Globus pallidus
Parkinson's disease
Progressive supranuclear palsy (tau)

Cerebellar nuclei (e.g. dentate nucleus)
Friedreich's ataxia
Spinocerebellar ataxia

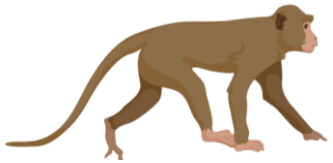
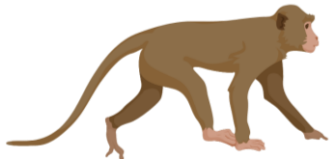
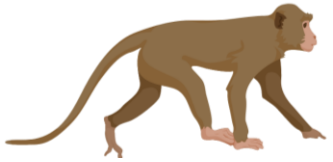
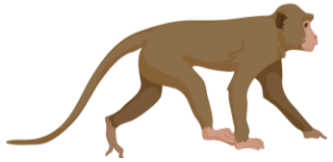
Brainstem (e.g. pons, substantia nigra)
Progressive supranuclear palsy (tau)
Rett syndrome
Parkinson's disease



Sangamo STAC-BBB findings exceeded expectations for a successful blood-brain barrier penetrant capsid

- STAC-BBB achieves robust penetration of the blood-brain barrier and **widespread distribution** throughout the brain
- Industry-leading performance: **700-fold better** enrichment than the benchmark AAV9
- Appears to **primarily target neurons** regardless of promoter
- Results are **consistent across individual animals and groups**
- Enables **robust expression** of zinc-finger cargo throughout the brain, including **all key brain regions**
- **Clear dose response curve** for both ZF expression and repression of the disease target
- Vector genomes are **enriched** in the CNS and appear de-targeted from the DRG and the liver
- We believe STAC-BBB is **manufacturable at scale**

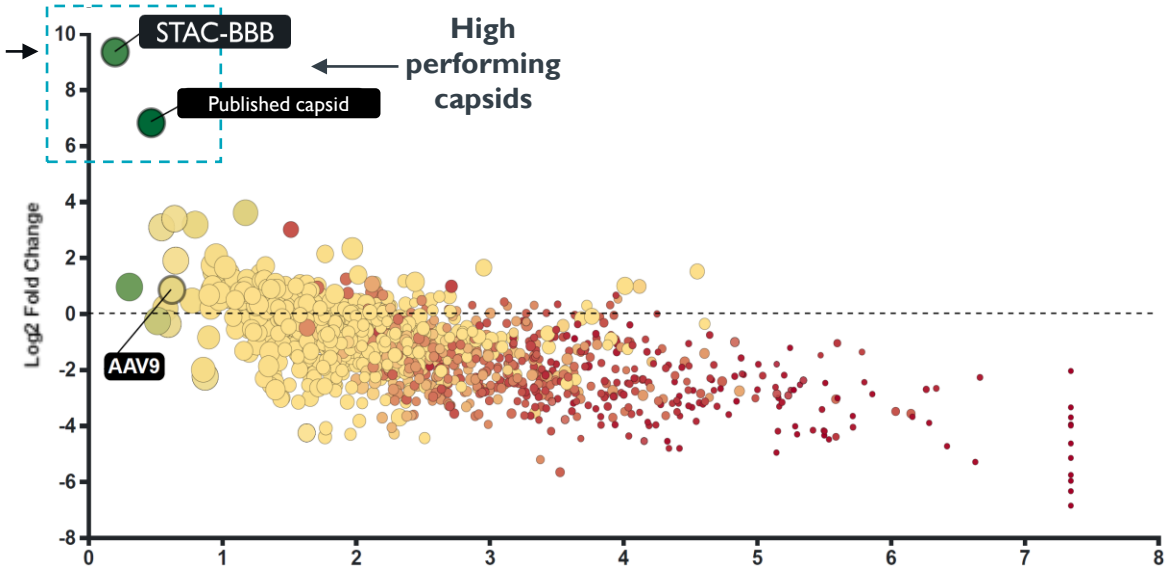
The SIFTER library screen has identified a leading blood-brain barrier penetrant capsid

Round 1	Round 2	Round 3	Individual evaluation
			
100 million capsids screened.	**60,000** capsids with sequence replicates. Includes controls with known performance.	**1,260** capsids with at least 4 unique sequence replicates. Includes controls with known performance.	**Single best** capsid variant (STAC-BBB) with reporter gene or therapeutically-relevant ZF cargo.

In vivo library evaluation in cynomolgus macaques identifies STAC-BBB as the top performing BBB-penetrant capsid for delivery to the brain

Capsid-mediated expression of cargo in neurons

644-fold enrichment in brain →



Log_2 Fold Change (Y-axis): Enrichment score relative to the administered library
Larger value is better

WHOLE BRAIN ASSESSMENT

Coefficient of Variation (X-axis): Variation in performance across tissue samples that were evaluated
Smaller value is better

5112
4544
3976
3408
2840
2272
1704
1136
568
1

Unique Molecular Identifier count (Color): Informs number of unique AAV transduction events
Darker green is better

Fraction of replicates found (Bubble size): Informs consistency of replicate recovery
Larger circle is better

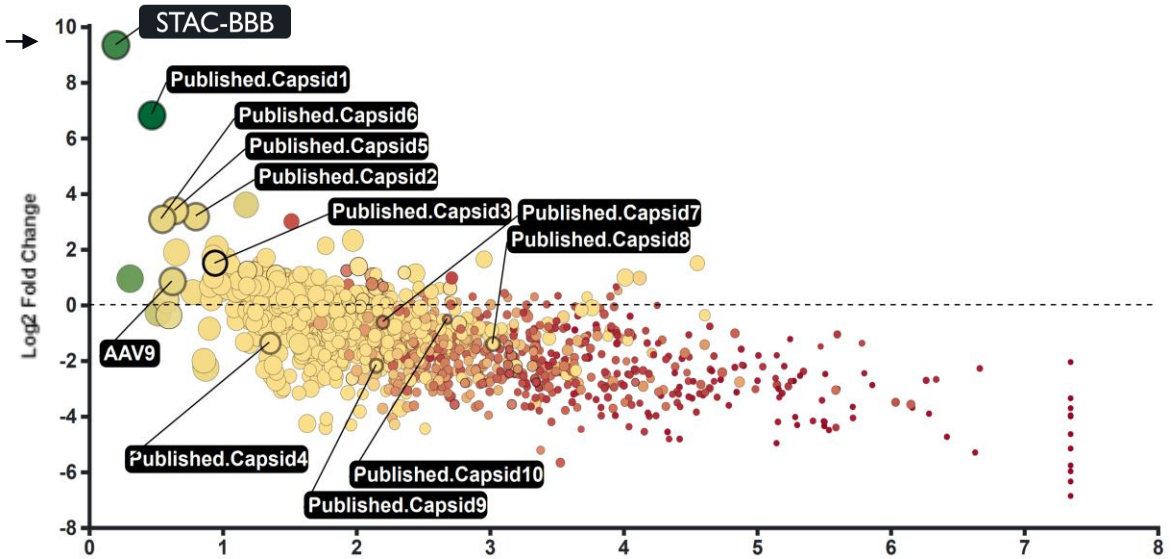
Neuronal RNA expression (3-week study, hSyn1)

Sangamo THERAPEUTICS

STAC-BBB outperforms other published CNS-tropic capsids

Capsid-mediated expression of cargo in neurons

644-fold enrichment in brain →



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WHOLE BRAIN ASSESSMENT

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Unique Molecular Identifier count (Color): Informs number of unique AAV transduction events **Darker green is better**

Fraction of replicates found (Bubble size): Informs consistency of replicate recovery **Larger circle is better**

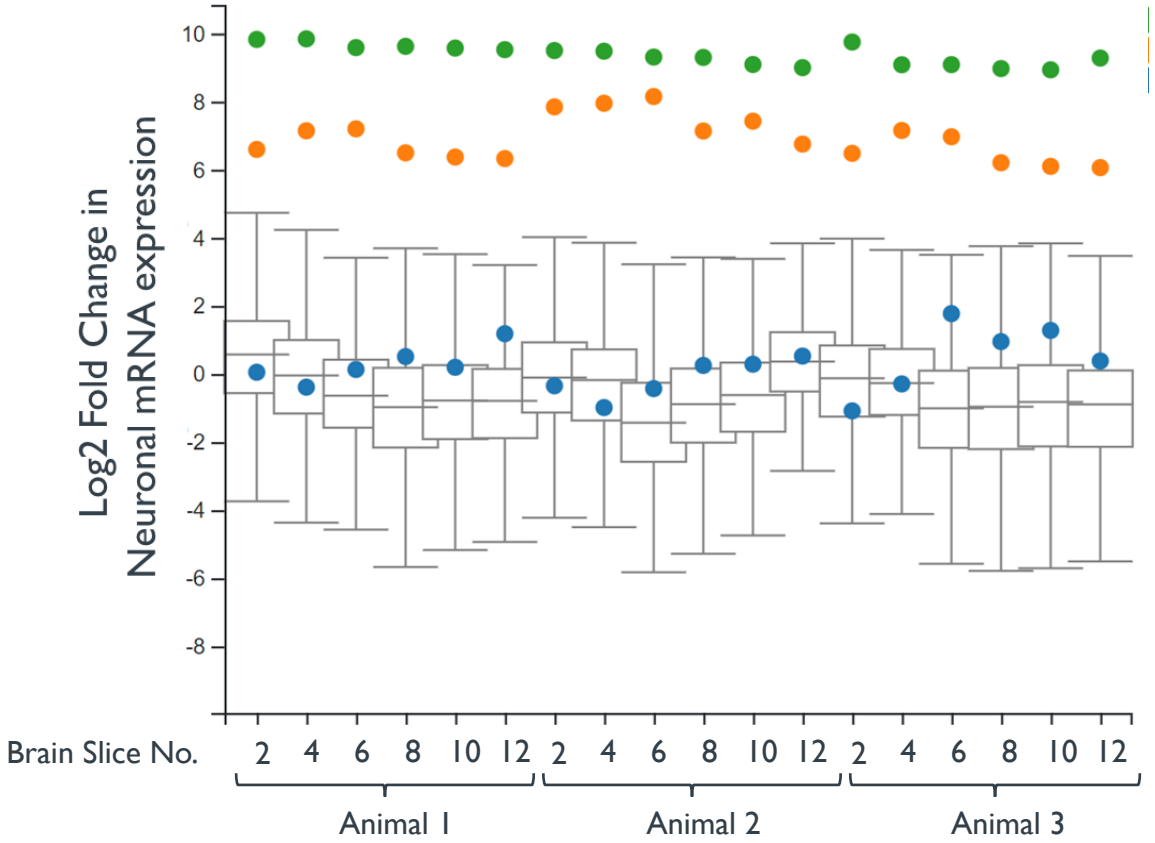
Neuronal RNA expression (3-week study, hSyn1)

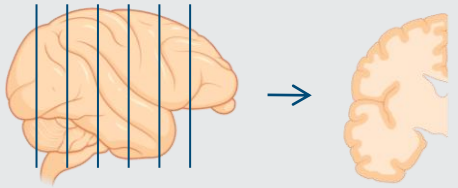
Sangamo THERAPEUTICS

STAC-BBB exhibits much higher neuronal RNA expression relative to AAV9 in all brain slices and all three animals

700-fold better enrichment than AAV9 and 5-fold better than the next best published capsid tested

Capsid-mediated expression of cargo in neurons





Assessment across brain slices and animals

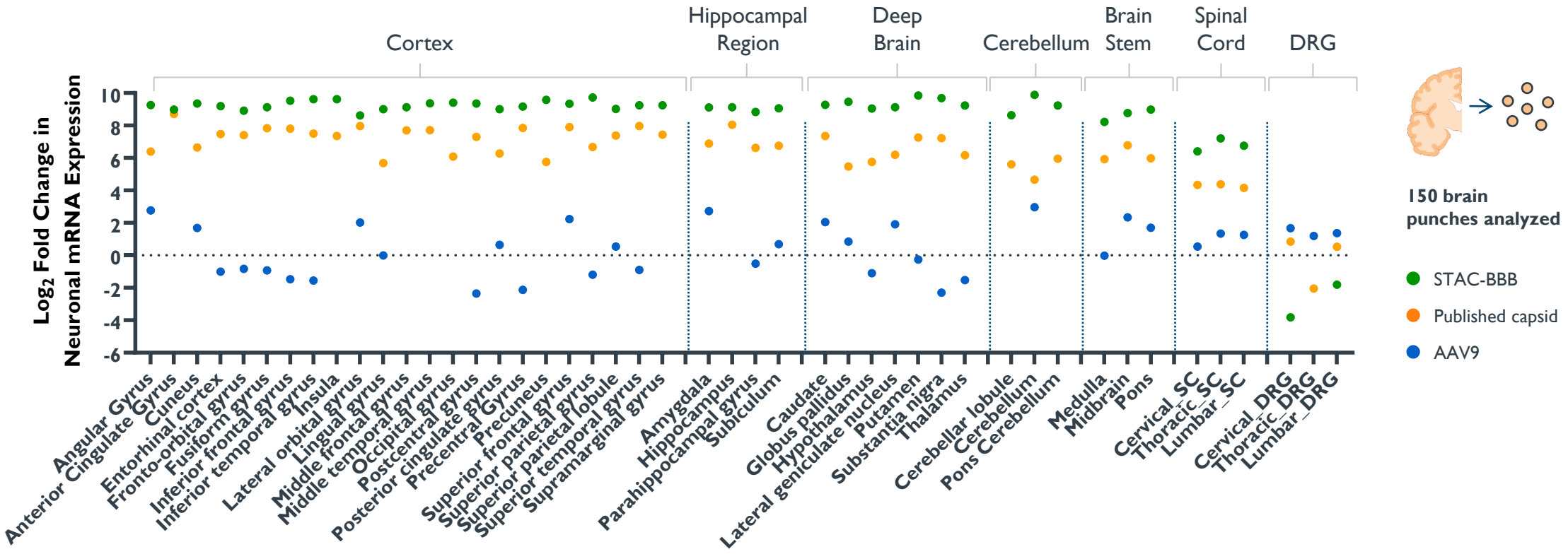
- STAC-BBB
- Published capsid
- AAV9

Neuronal RNA expression (3-week study, hSyn1)
Box represents 25th – 75th percentile of library performance. Whiskers are 1.5x the interquartile range.

Sangamo THERAPEUTICS

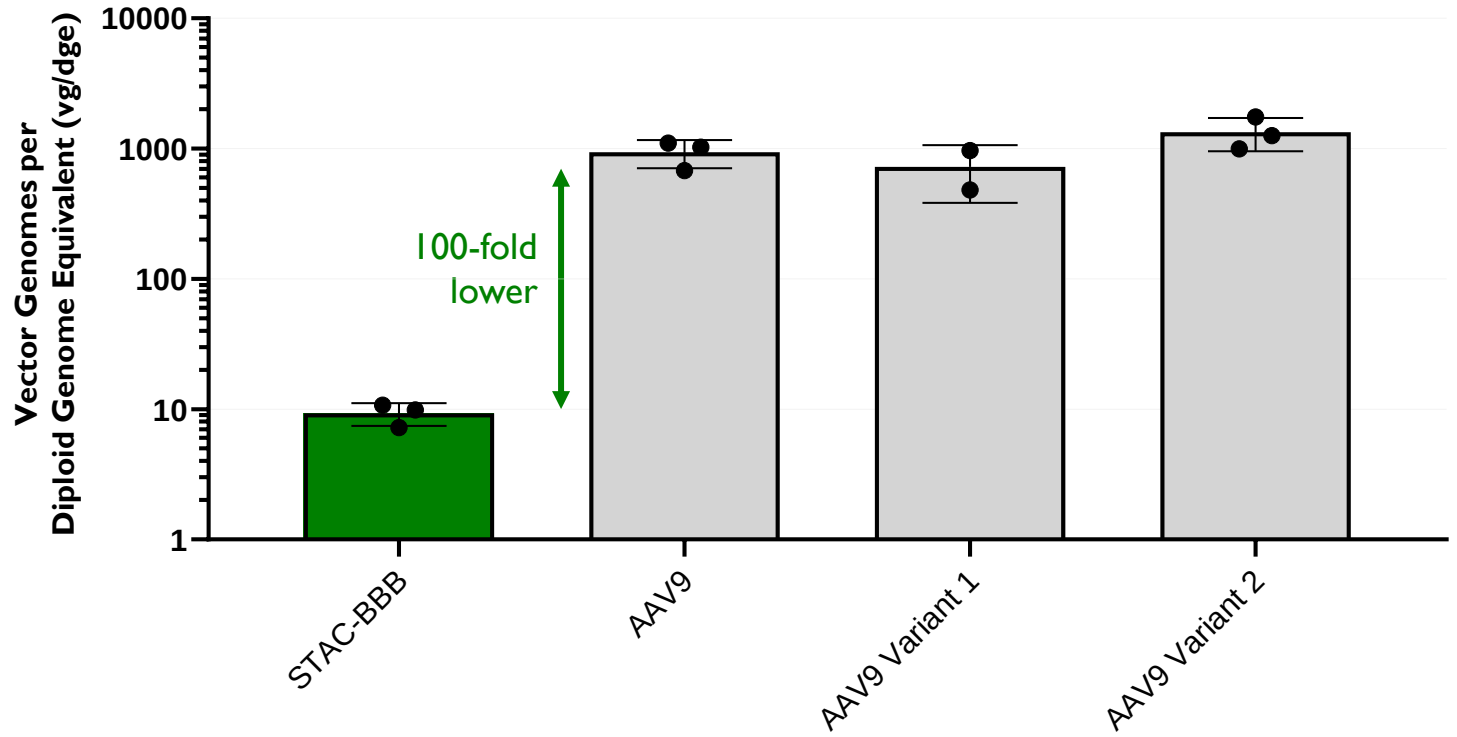
STAC-BBB is enriched in neuronal RNA expression in all CNS regions

Capsid-mediated expression of cargo in neurons



Neuronal RNA expression (3-week study, hSyn1)

STAC-BBB exhibits profound liver de-targeting relative to AAV9



Comparison is relative to historical Sangamo studies, all data shown is for a 1e14 vg/kg dose

High liver exposure after intravenous administration is a limitation of conventional AAV serotypes including AAV9

STAC-BBB achieves efficient CNS delivery while maintaining low peripheral exposure in liver and dorsal root ganglia (DRG)

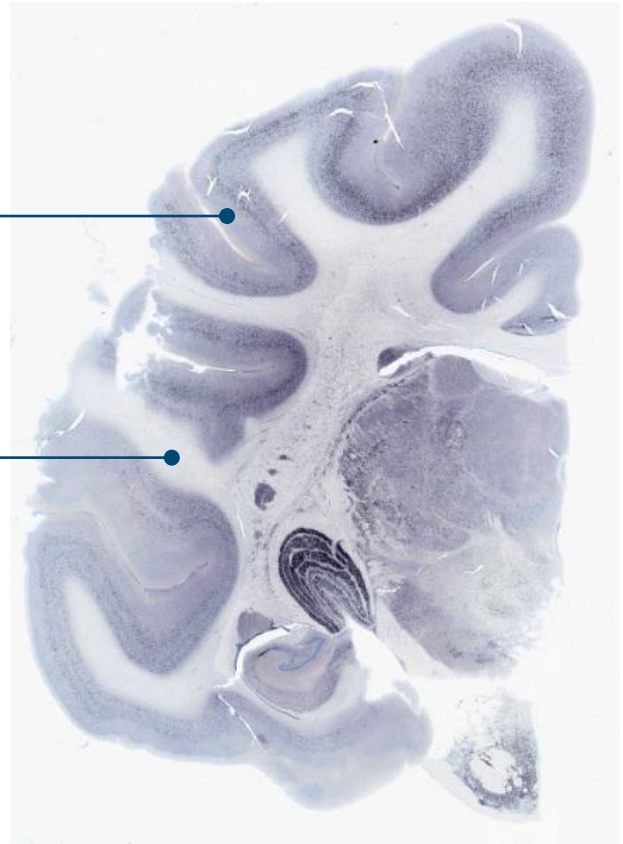
This is the ideal profile for a CNS-targeted capsid

STAC-BBB drives widespread and robust expression throughout the brain

Grey matter (cell bodies)

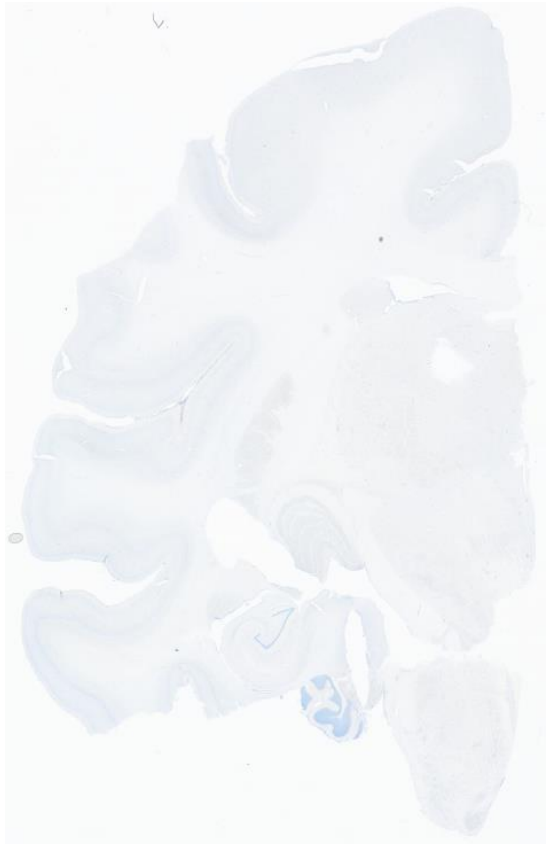
White matter (nerve fibers)

STAC-BBB
(Nuclear-localized GFP)



2e13 vg/kg STAC-BBB, 19 days post administration

Negative control
(no AAV treatment) – No signal



Nissl staining (light blue):

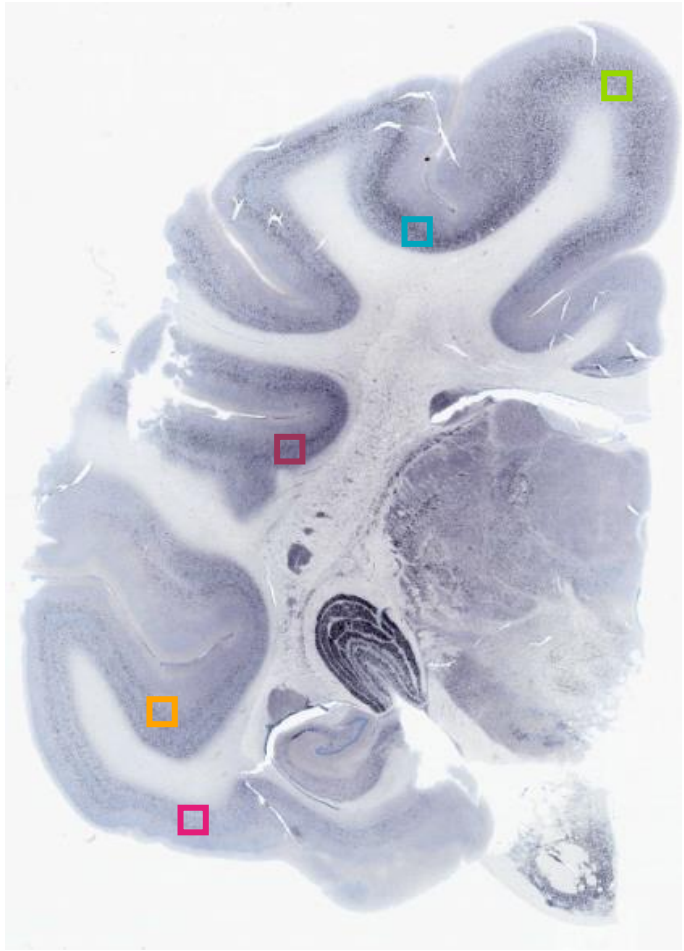
All cell nuclei

Antibody labeling for green florescent protein (GFP) expression (black):

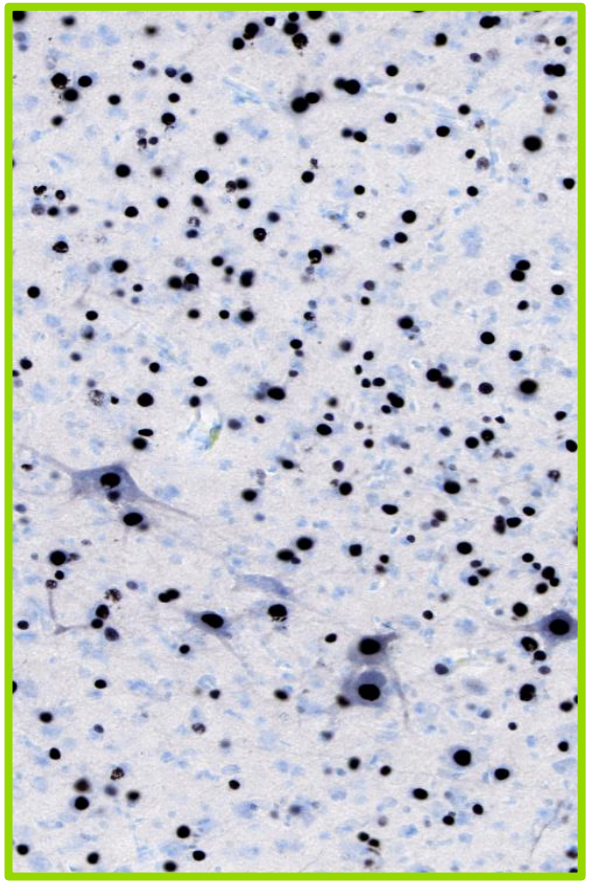
Cells transduced with STAC-BBB

Sangamo THERAPEUTICS

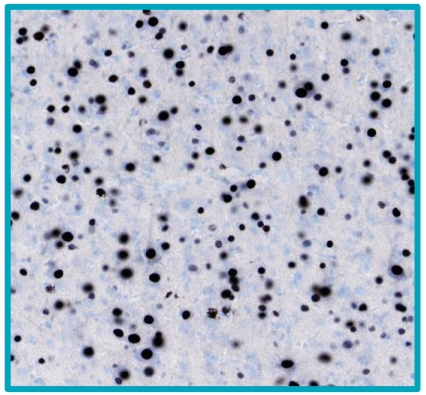
STAC-BBB shows widespread neuronal transduction across all cortical regions



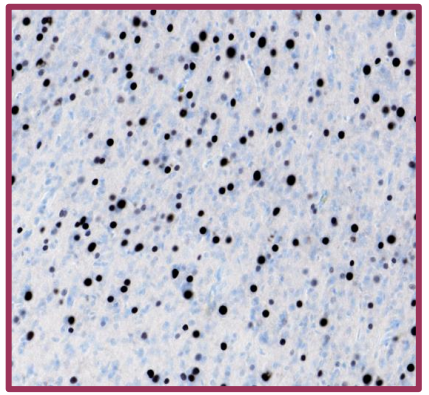
Precentral Gyrus (Motor Cortex)



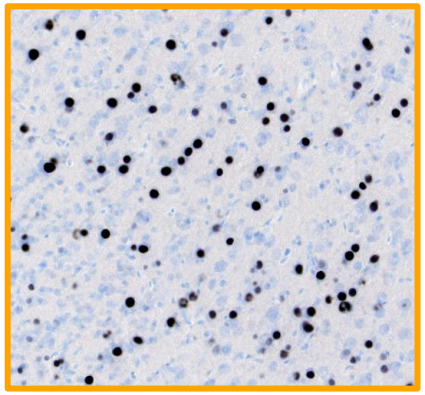
Postcentral Gyrus



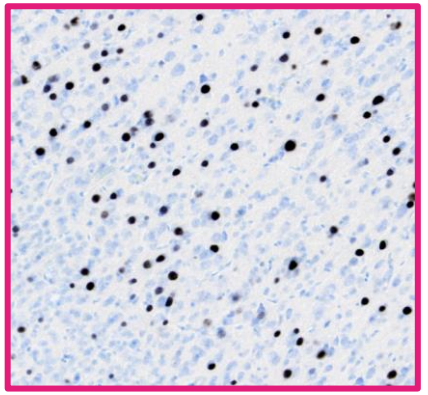
Superior Temporal Gyrus



Middle Temporal Gyrus

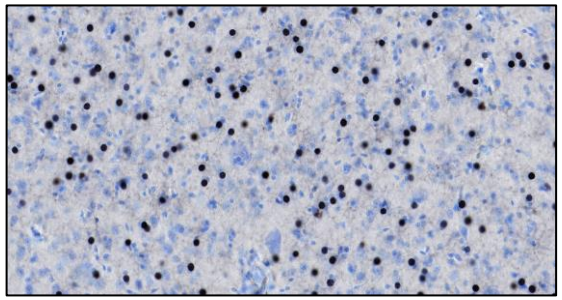


Inferior Temporal Gyrus

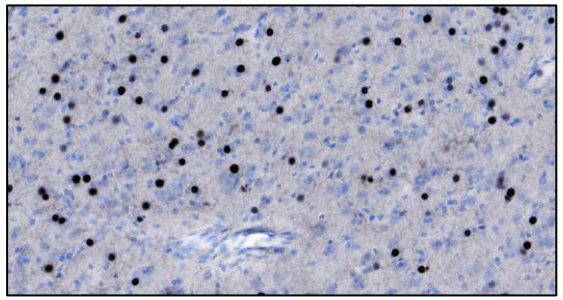


STAC-BBB mediates widespread brain transduction at the 2e13 vg/kg dose

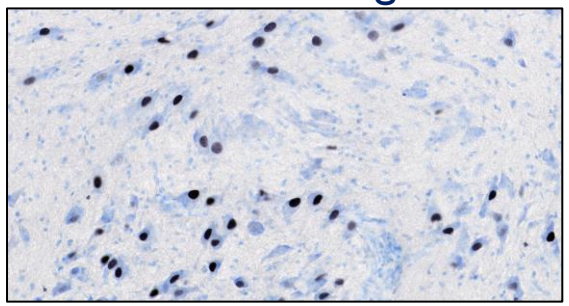
Putamen



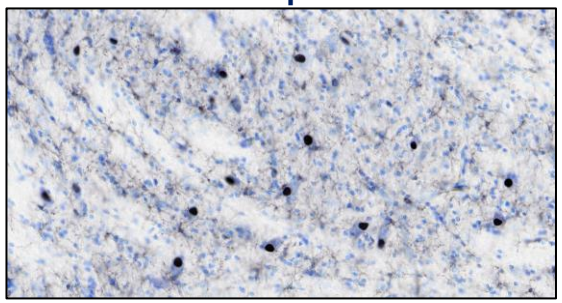
Caudate



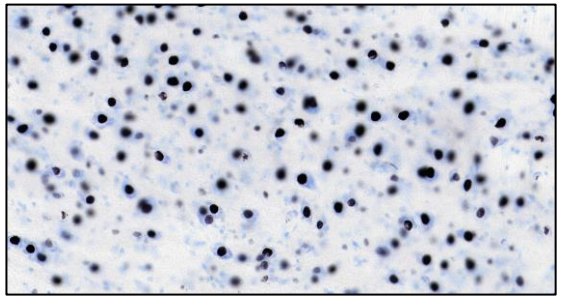
Substantia nigra



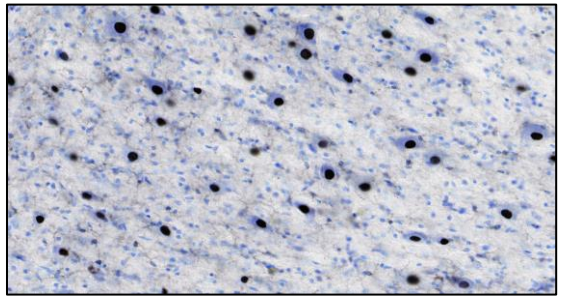
Globus pallidus



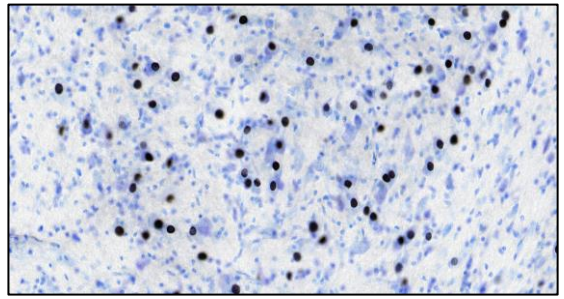
Pons



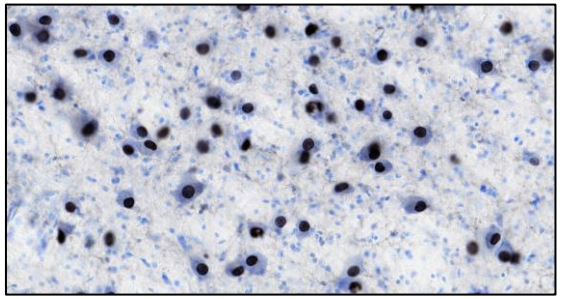
Dentate nucleus



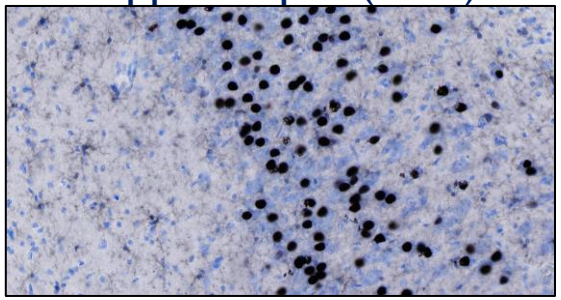
Cuneate nucleus



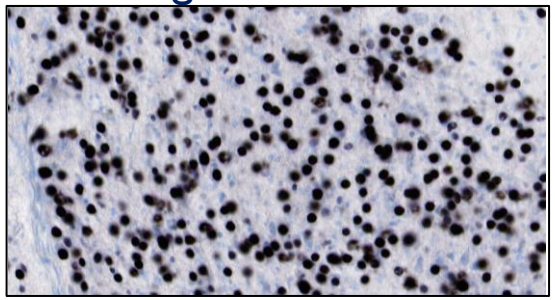
Thalamus



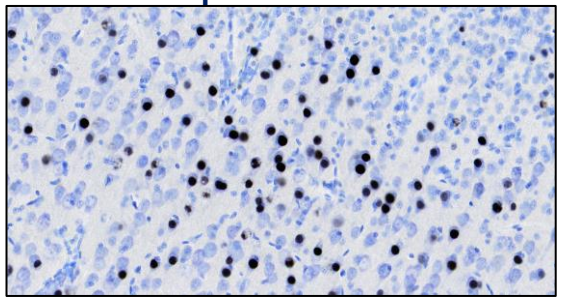
Hippocampus (CA2)



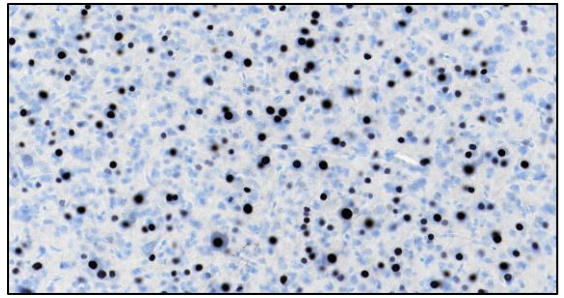
Lateral geniculate nucleus



Temporal cortex



Motor cortex



Sangamo THERAPEUTICS

2e13 vg/kg STAC-BBB, 19 days post administration

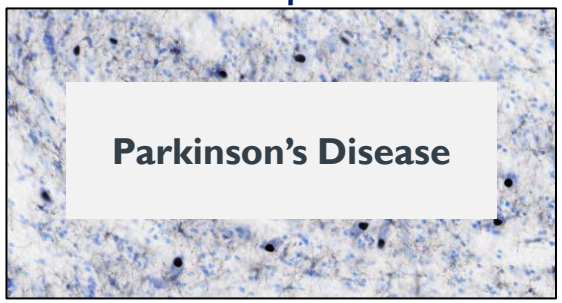
Neurons are widely transduced in regions integral to disease pathology

Putamen

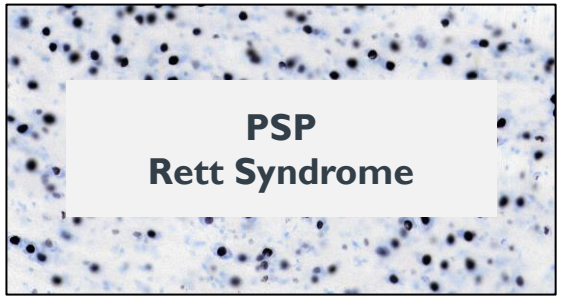
Caudate

Substantia nigra

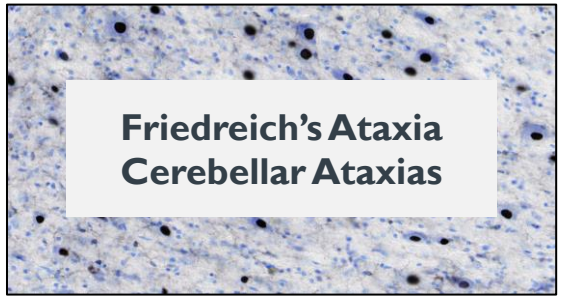
Globus pallidus



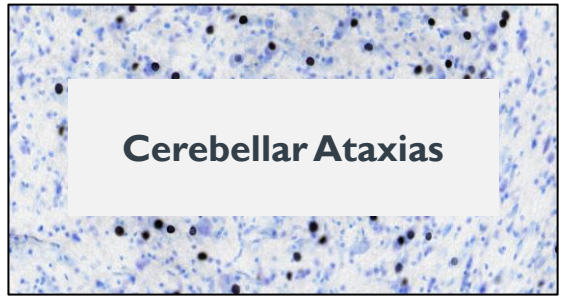
Pons



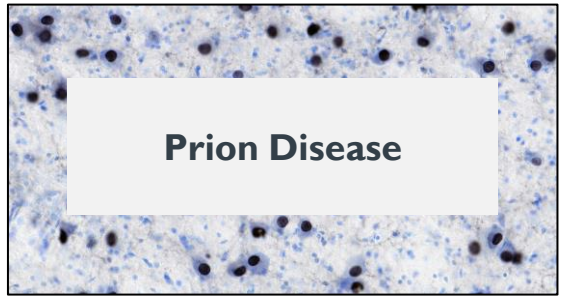
Dentate nucleus



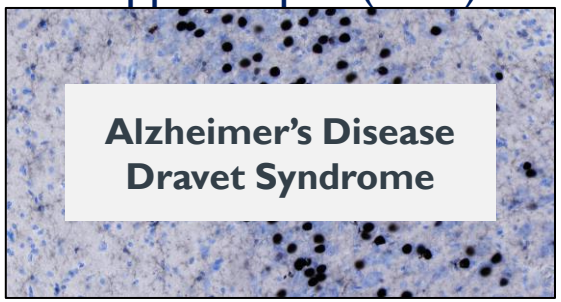
Cuneate nucleus



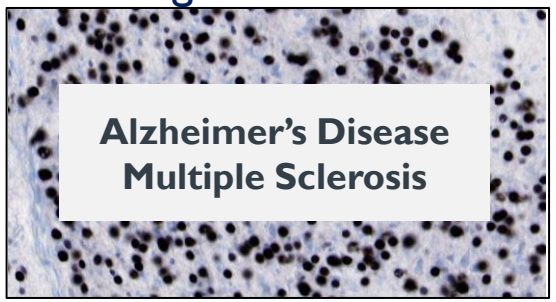
Thalamus



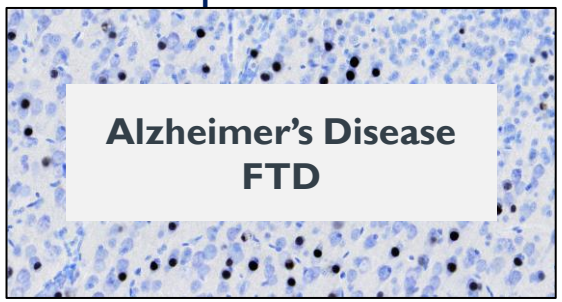
Hippocampus (CA2)



Lateral geniculate nucleus



Temporal cortex



Motor cortex

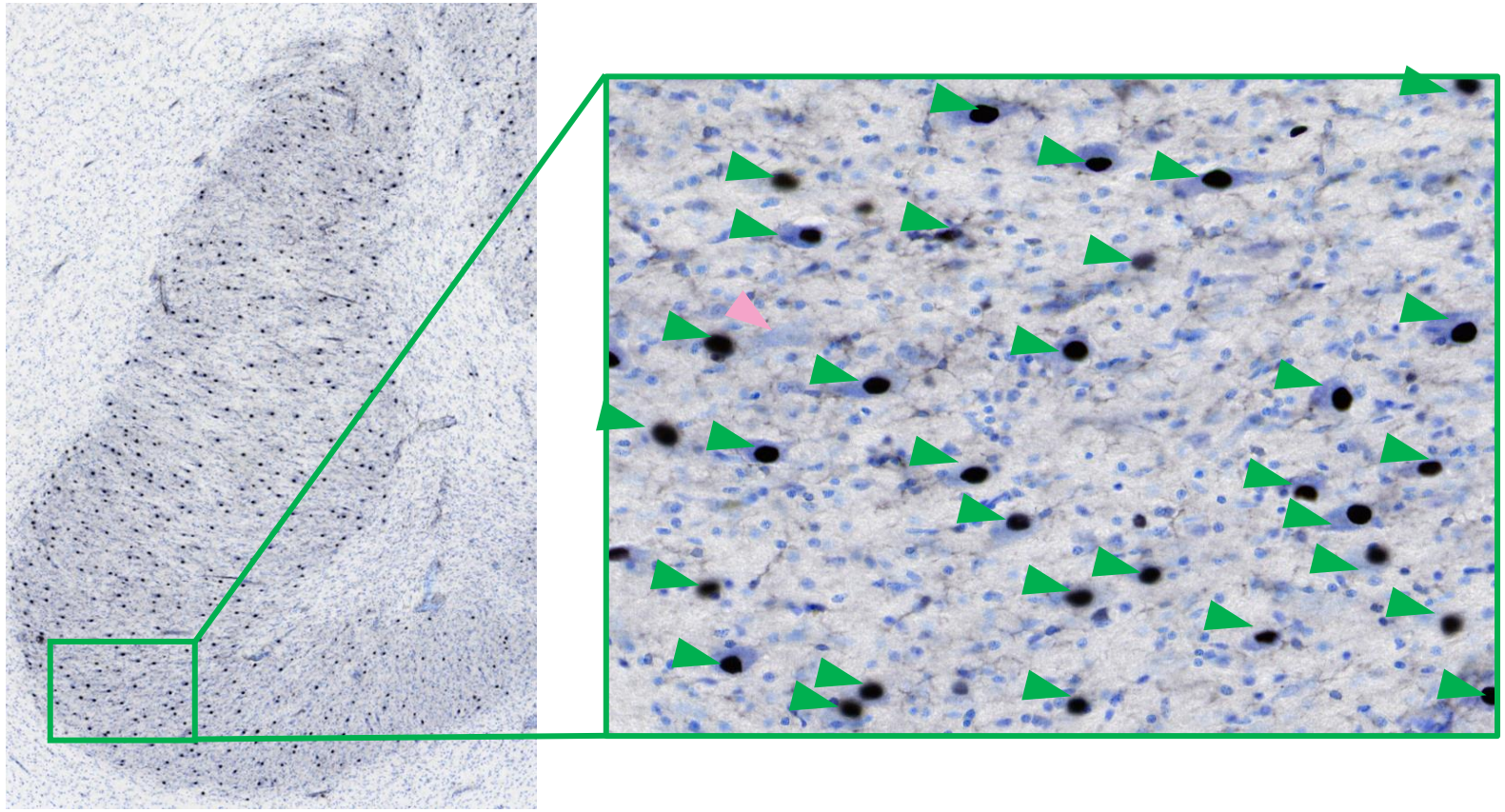
ALS: Amyotrophic lateral sclerosis; FTD: Frontotemporal dementia; PSP: Progressive supranuclear palsy
2e13 vg/kg STAC-BBB, 19 days post administration

Sangamo THERAPEUTICS

Nearly all neurons in the dentate nucleus are transduced by STAC-BBB

Dentate nucleus - disease targets: Friedreich's ataxia, Spinocerebellar ataxias

30 out of 31 neurons visible in this field are transduced



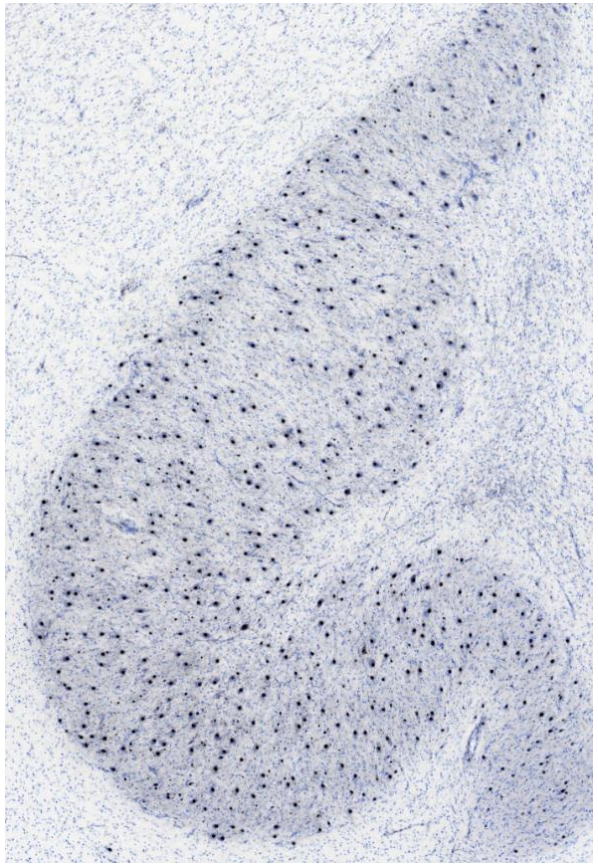
Neuronal nuclei

- Transduced
- Not transduced

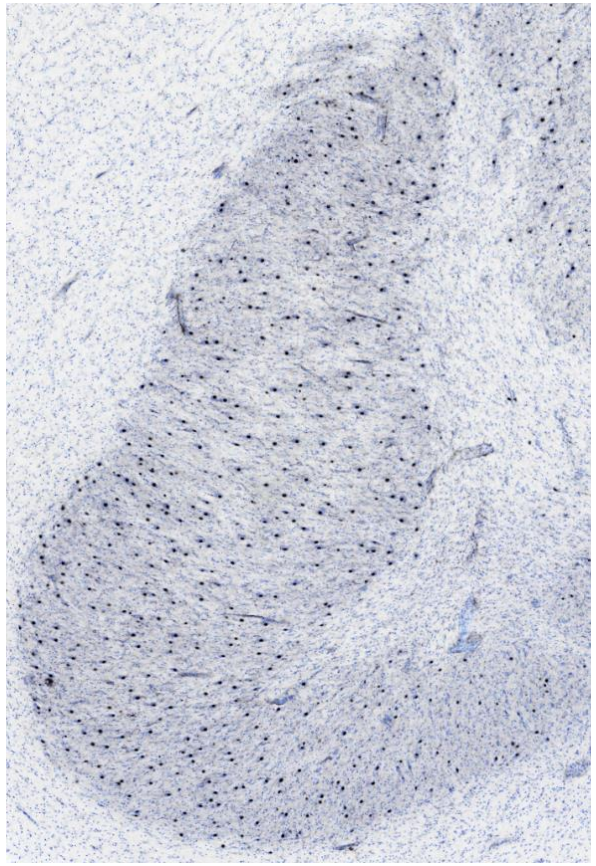
2e13 vg/kg STAC-BBB, 19 days post administration

Consistency in transduction is observed across all animals

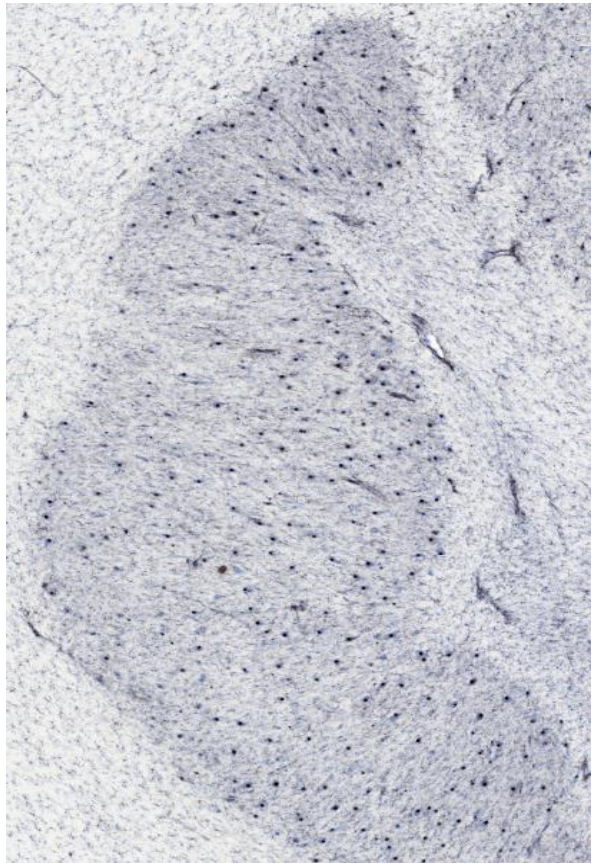
Dentate nucleus - disease targets: Friedreich's ataxia, Spinocerebellar ataxias



NHP 1



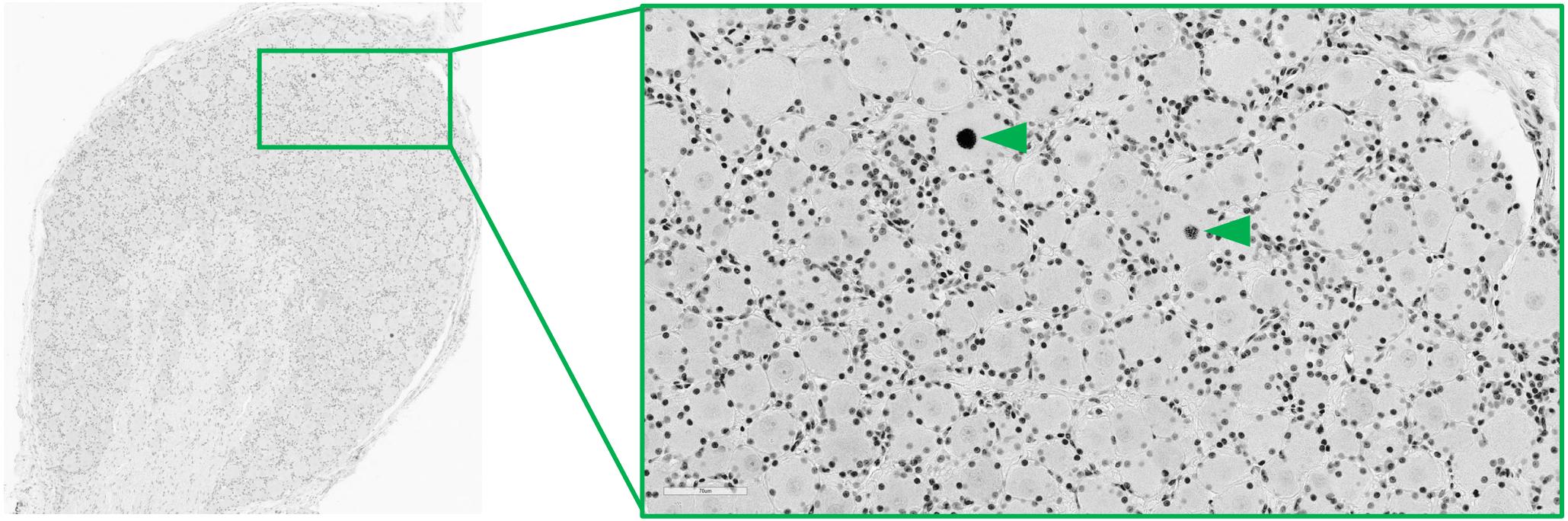
NHP 2



NHP 3

2e13 vg/kg STAC-BBB, 19 days post administration

Desired de-targeting of the dorsal root ganglia is observed



Minimal delivery to dorsal root ganglia is desirable for an intravenously administered AAV capsid

Sensory neurons are the large cell bodies in this image

STAC-BBB shows very little delivery to these sensory neurons, especially relative to the level of CNS targeting observed

2e13 vg/kg STAC-BBB, 19 days post administration

We believe STAC-BBB is manufacturable at scale

- Capsid manufacturability is critical to create a successful potential commercial drug product for patients
- We believe STAC-BBB is:
  - Manufacturable at commercial scale using standard cell culture and purification processes
  - Soluble using known excipients
  - Can be characterized using available analytics
- We have successfully manufactured up to 50-liter scale, and further scale up to 500-liter is in progress

Sangamo THERAPEUTICS

Delivering Versatile Zinc Finger Payloads Throughout the CNS

Sangamo has the tools needed to advance a next-generation neurology genomic medicine company

Highly Potent Zinc Finger Cargo

Level of potency is precisely customizable to the indication being targeted

Versatility and Exquisite Specificity

We believe any gene in the genome is targetable for up- or down-regulation

All Human Derived

Potentially avoids issues with immunogenicity

Small Size. Easily Packaged.

Zinc fingers can be easily packaged into viral vectors

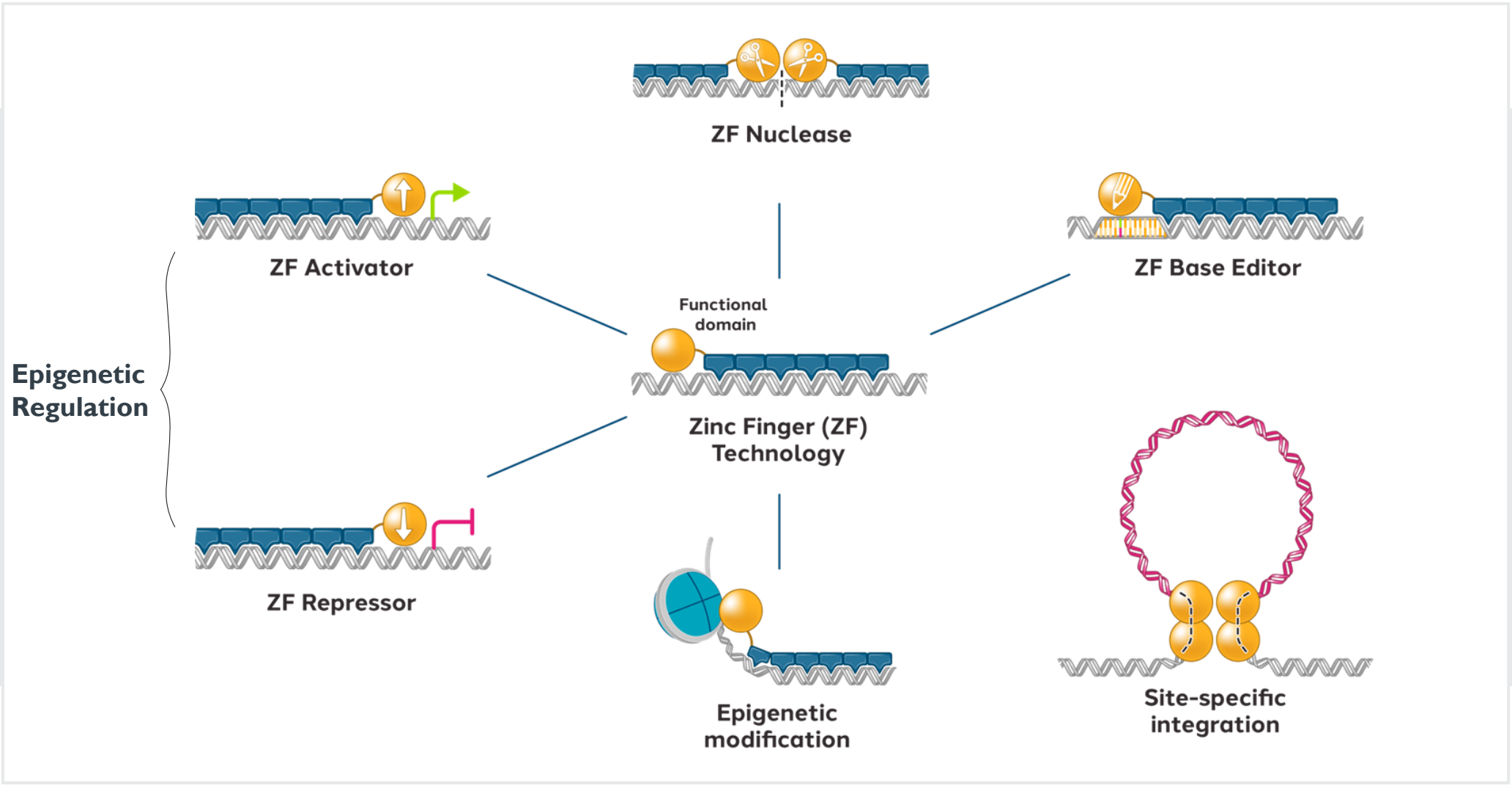
Powerful AAV Delivery Platform

Widespread zinc-finger 'cargo' delivery – via both intravenous AND intrathecal delivery

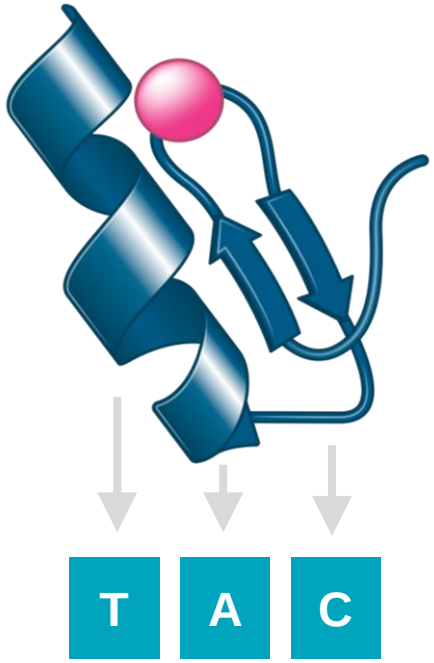
Potentially Industry Leading CNS Tropism

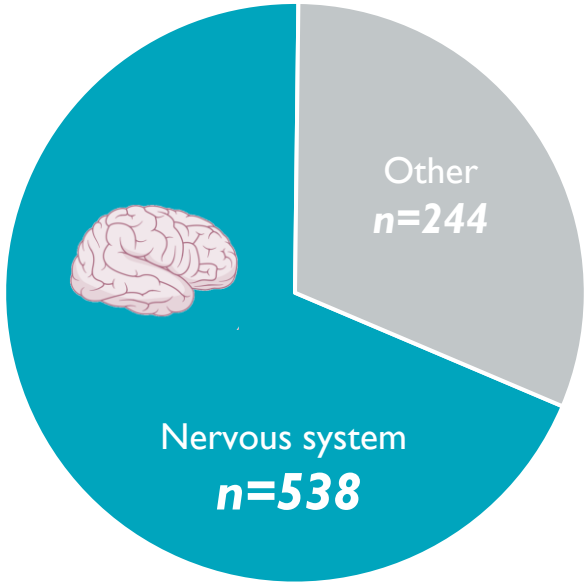
Robust penetration of the blood-brain barrier and widespread distribution throughout the brain

Sangamo's differentiated genomic engineering platform is flexible, creating specific tools for the needs of each target

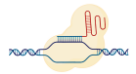


Zinc finger epigenetic regulators are the ideal cargo for neurology-focused genomic medicines









	ZFR/ZFA	ASO	CRISPR
Single administration	✓	✗	✓
Human derived	✓	✗	✗
Target any sequence	✓	✗	✗
Cell-type specificity	✓	✗	~
Compact / multiplexing	✓	~	✗
Supplement with cDNA	✓	✗	✗
All RNA / protein forms	✓	~	✓
Allele specific	✓	✗	~

Zinc Fingers are natural proteins that bind DNA with high specificity

At least 782 human genes encode Zinc Finger Proteins

Most regulate the epigenetic state of other genes

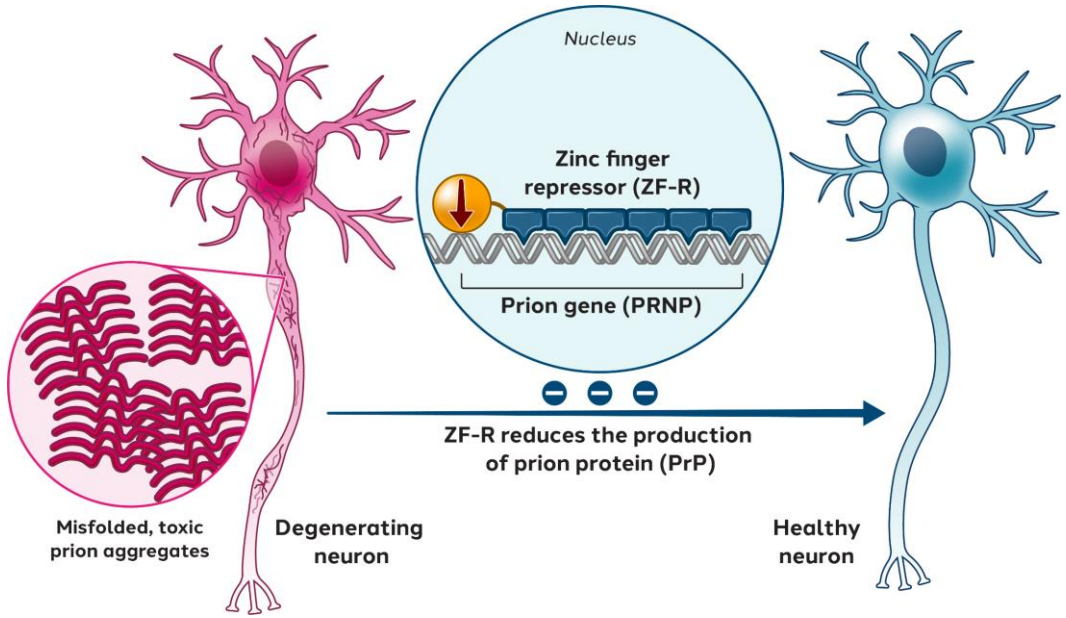
Zinc fingers are differentiated in key therapeutic features for treating neurologic diseases

n=782 C2H2 ZF-containing genes
Sources: Ensembl human genes; GTEx: CNS (>5 TPM)
ASO: antisense oligonucleotide

Sangamo THERAPEUTICS

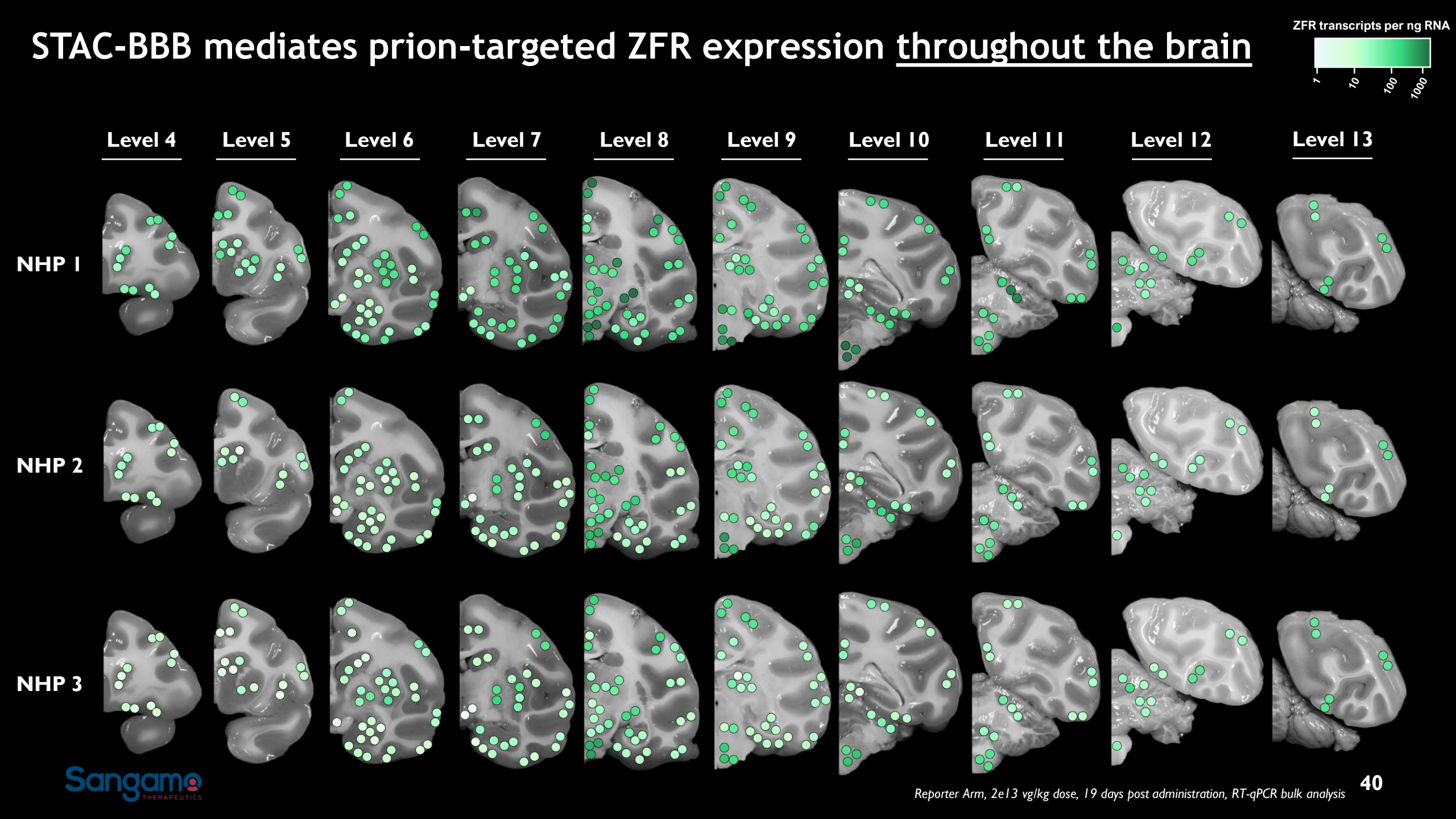
Prion disease is rapidly progressive and always fatal

Rapid path to clinical validation in a devastating disease with no current approved treatment options. Clear regulatory path and efficacy endpoints. Unlocks additional neurodegenerative indications.



- Progressive condition, with **no disease modifying therapy**
- Sporadic, inherited and acquired forms
- Very **well-defined** patient population
- Symptoms can include **cognitive, psychiatric and motor deficits**
- **Excellent fit** for a ZF repression approach
  - Prion knockout animals do not get disease
  - Prion reduction can delay or prevent disease
  - Neuronal PrP reduction prevents disease
- Repression of prion expression in the brain **may slow or halt disease progression and neurodegeneration**

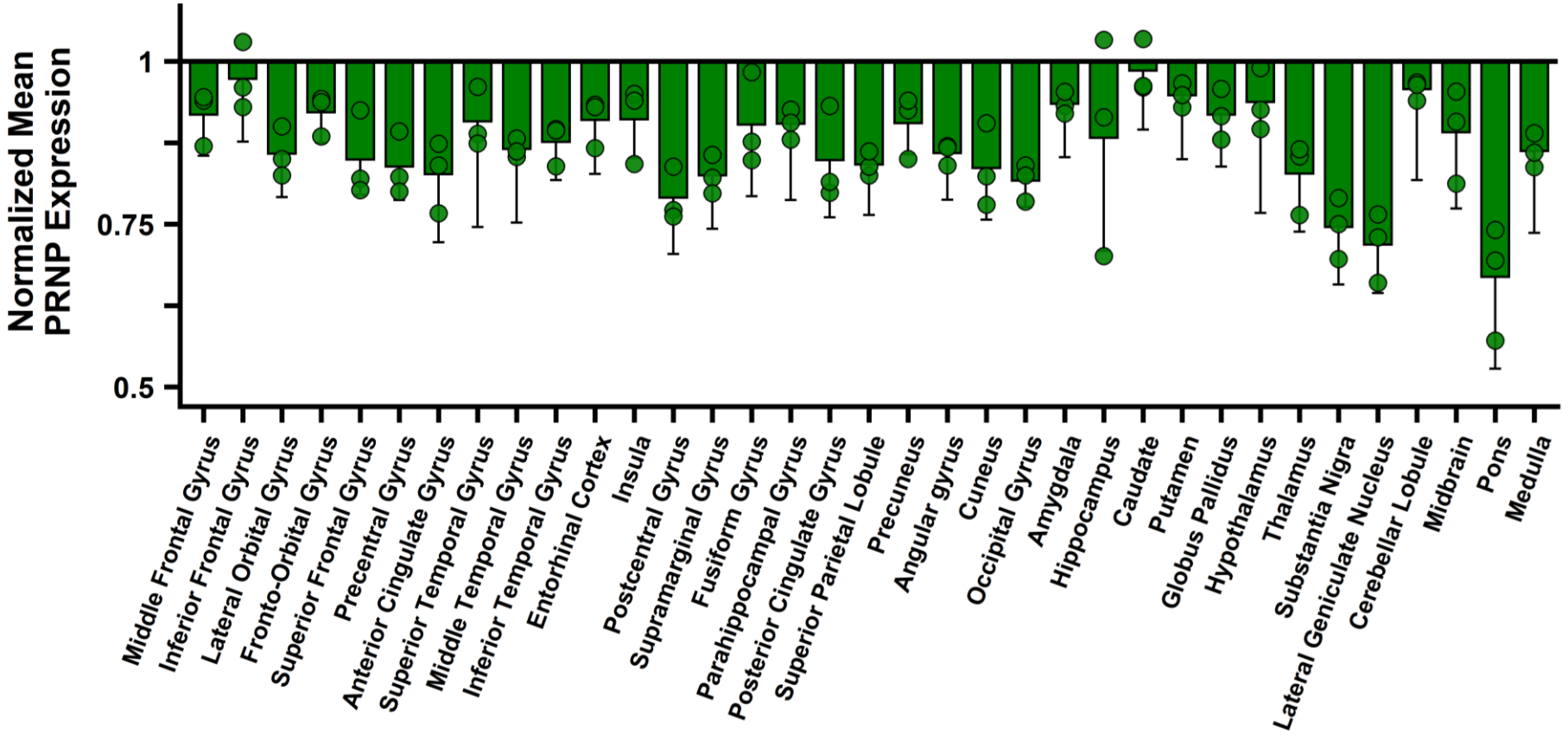
STAC-BBB mediates prion-targeted ZFR expression throughout the brain



Reporter Arm, 2e13 vg/kg dose, 19 days post administration, RT-qPCR bulk analysis

STAC-BBB mediated ZFR expression translates to brain-wide prion repression in all 35 brain regions analyzed

Prion gene expression, 19 days post administration, bulk analysis



← Prion expression in control animals is set to 1

STAC-BBB

2e13 vg/kg

Data analyses bulk brain punches.

Each bar is average of 3 animals.

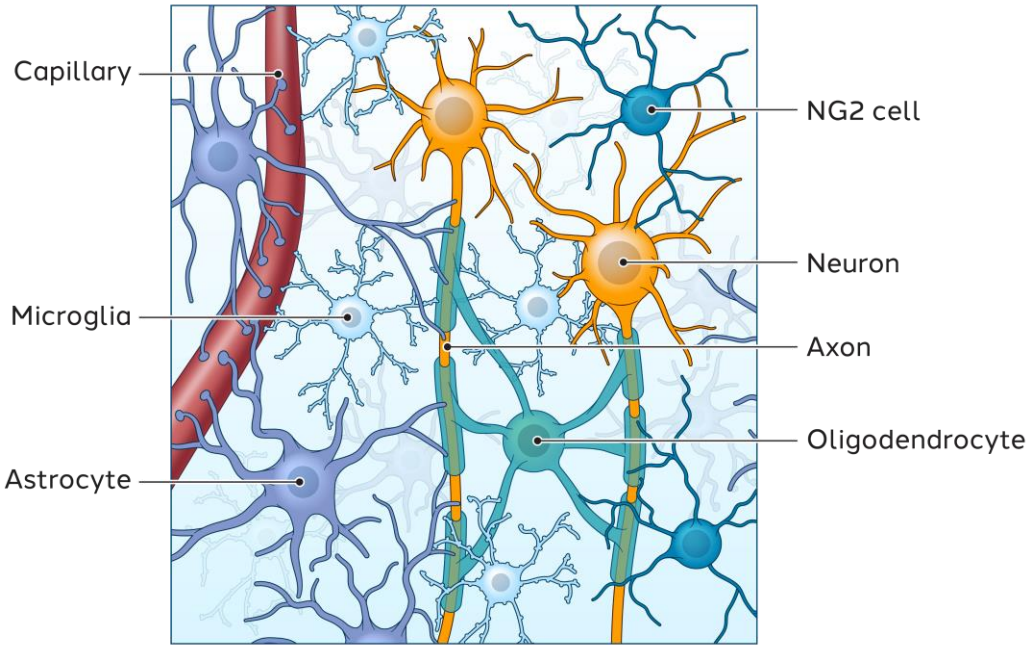
Each dot represents the average of multiple brain punches for one animal for the indicated region.

Genomic medicines enable cell-type specificity, critical for efficacy and safety when treating neurological diseases

Framework for understanding 'bulk analyses'

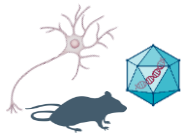
- Cell-type-specific promoters drive zinc finger expression **exclusively in neurons**
- Neurons are **critical drivers of disease pathology**, and key therapeutic targets
  - Non-neuronal cell types often express a gene involved in a disease, but either do not make the protein OR are not the disease drivers
- Neurons only make up **a percentage of overall** brain cell types (19-40%)
- This creates a **'floor effect'** for bulk analysis data due to the selectivity of our approach for gene repression in neurons

Prior experiments tell us even modest target repression in bulk brain tissue can lead to significant changes in disease progression

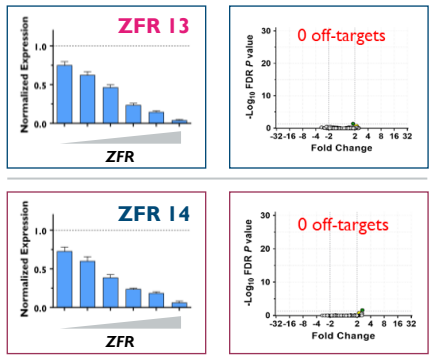


Zinc finger repressors extend survival in a mouse model of aggressive prion disease

Potent and specific ZFRs

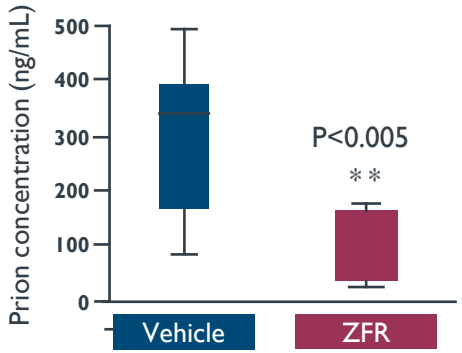


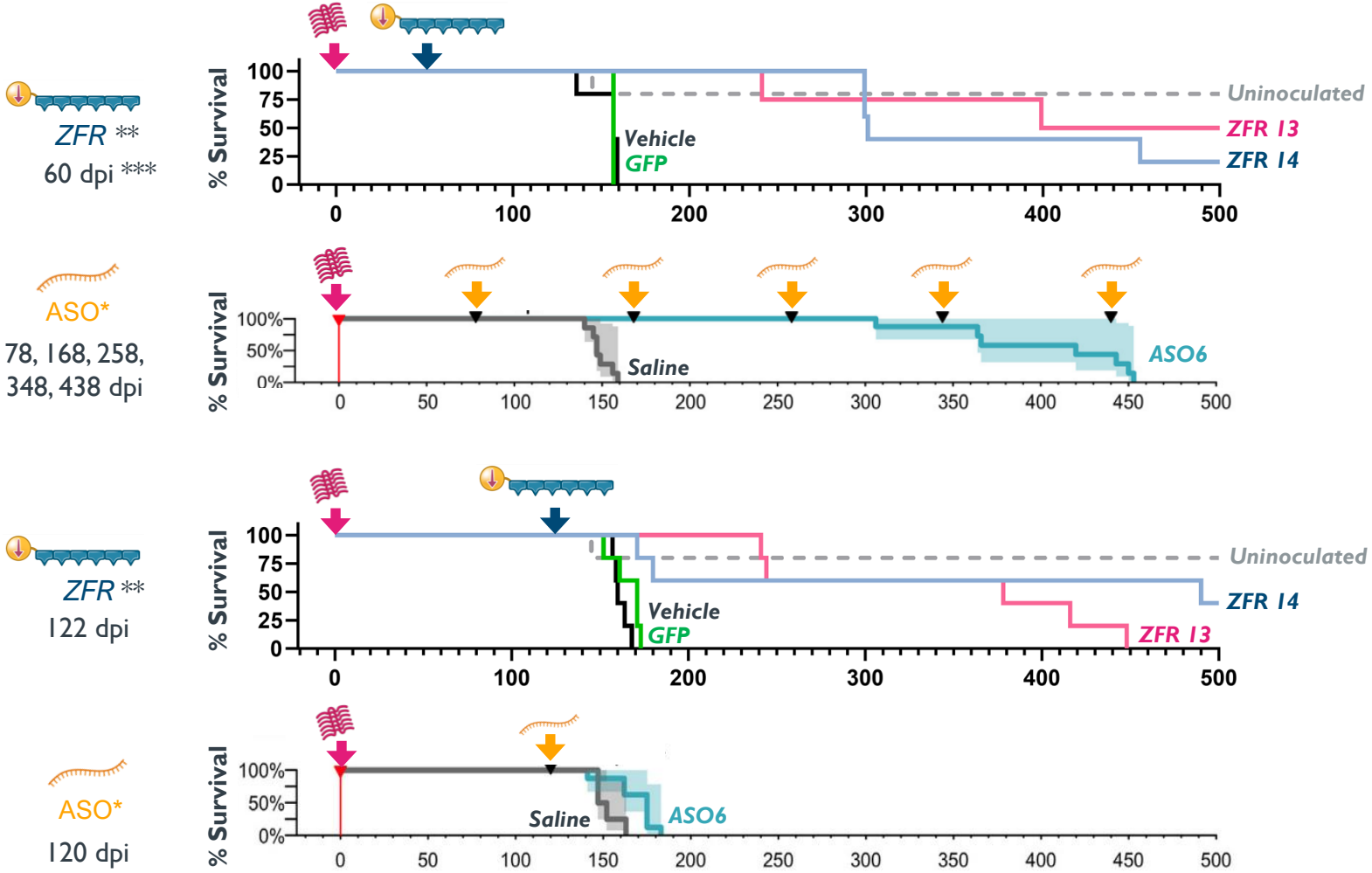
Primary neurons



Reduction of CSF biomarker

CSF





Sangamo THERAPEUTICS

Data presented at ASGCT 2023

** ASO Data from Minikel et al 2020*
*** ZFR administered intravenously using PHPB capsid*
**** dpi: days post infection*

The prion program is rapidly progressing, with CTA submission expected in 2025

Summary

- Clinical lead ZFR with >95% prion reduction per cell, no off-targets, and exceptional potency *in vitro* and *in vivo*
- Target engagement, durability and safety demonstrated in mouse and NHP studies
- Best-in-disease efficacy in gold standard survival model (Misfolded PrP^{Sc} infected mice)
- GLP toxicology study planned for H2'2024. CTA submission expected Q4 2025*.

Activity, Status	 ZFR design, screening	 In vitro validation	 Rodent TE, safety	 Rodent efficacy	 NHP TE, safety	 NHP GLP/TOX	**CTA Q4 2025***
Models	Human cell line Mouse cell line Human fibroblasts	Human iPSC neurons Mouse neurons	Wildtype mice *hPRNP* mice	PrP^{Sc} survival model @ -21, 60, or 120 days post infection	Cynomolgus NHP, IV administration		
Endpoints	*PRNP* mRNA Transcriptomics	*PRNP* mRNA Transcriptomics PrP protein	*PRNP* mRNA Transcriptomics PrP protein (tissue) PrP protein (CSF) Single-cell ISH/IHC Tolerability	Survival Plasma NfL PrP pathology *PrP* mRNA & protein Single-cell ISH/IHC Safety/pathology	*Prnp*, ZFR mRNA Single-cell ISH/IHC Biodistribution Safety/pathology		

** Subject to our ability to secure adequate funding*

Sangamo THERAPEUTICS

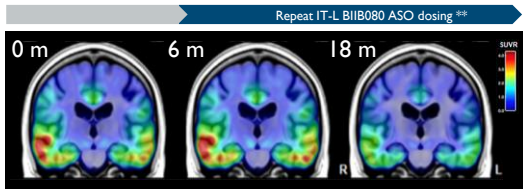
Neurodegenerative diseases, driven by tau pathology, impact millions of people globally

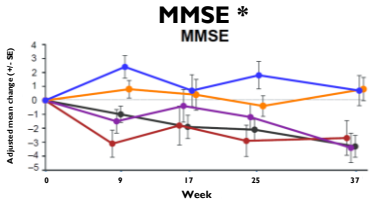
Leverages STAC-BBB delivery capsid. Targets a very large patient population with high unmet medical need. Unlocks multiple tauopathy indications, in addition to Alzheimer's disease.

Tauopathy disorders span indications including:

- AD – Alzheimer's disease
- PSP – Progressive supranuclear palsy
- FTD – Frontotemporal dementia
- CTE – Chronic traumatic encephalopathy
- CBS – Corticobasal syndrome
- LBD – Lewy body disease (+ alpha synuclein)

Lowering tau expression can reverse established tau pathology and potentially halt AD progression in humans





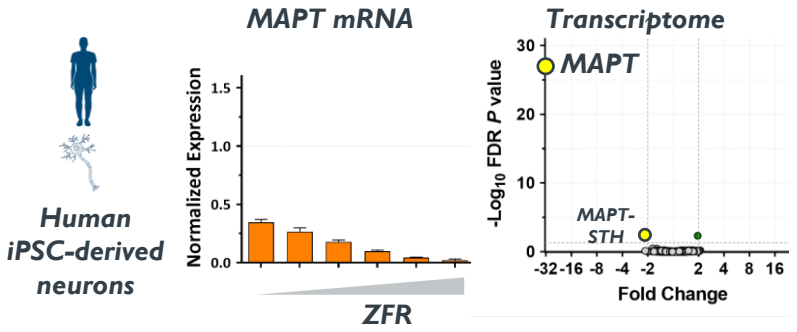
Sangamo's approach is differentiated in several important ways

	ZFR	ASO
All tau forms targeted at the source, inside neurons	✓	✓
One-time, IV administration	✓	✗
All brain regions = all tauopathy indications	✓	✗
Cell-type specificity, restricted to CNS cell types	✓	✗
Rapid pharmacokinetics, 100% single-cell potency	✓	✗

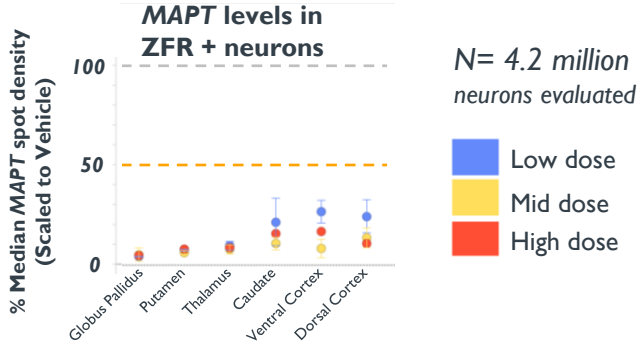
* *Biogen, Clinical Trials in Alzheimer's Disease (CTAD) 2023*
** *Ionis October 2023 Innovation Day*

In prior experiments via direct injection, tau clinical lead ZFR achieved potent, but focal tau reduction in NHPs

>95% mRNA repression and exceptional specificity



Potent, focal tau repression in NHP



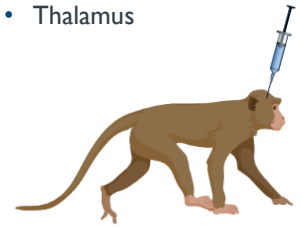
N= 4.2 million neurons evaluated

- Low dose
- Mid dose
- High dose

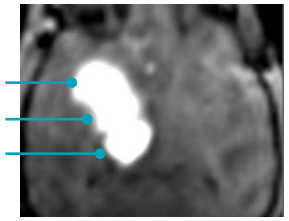
- >90% single-cell *MAPT* repression in ZFR+ neurons
- Some diffusion and trafficking to distal sites
- ~50% coverage of each targeted region

Targets for direct injection:

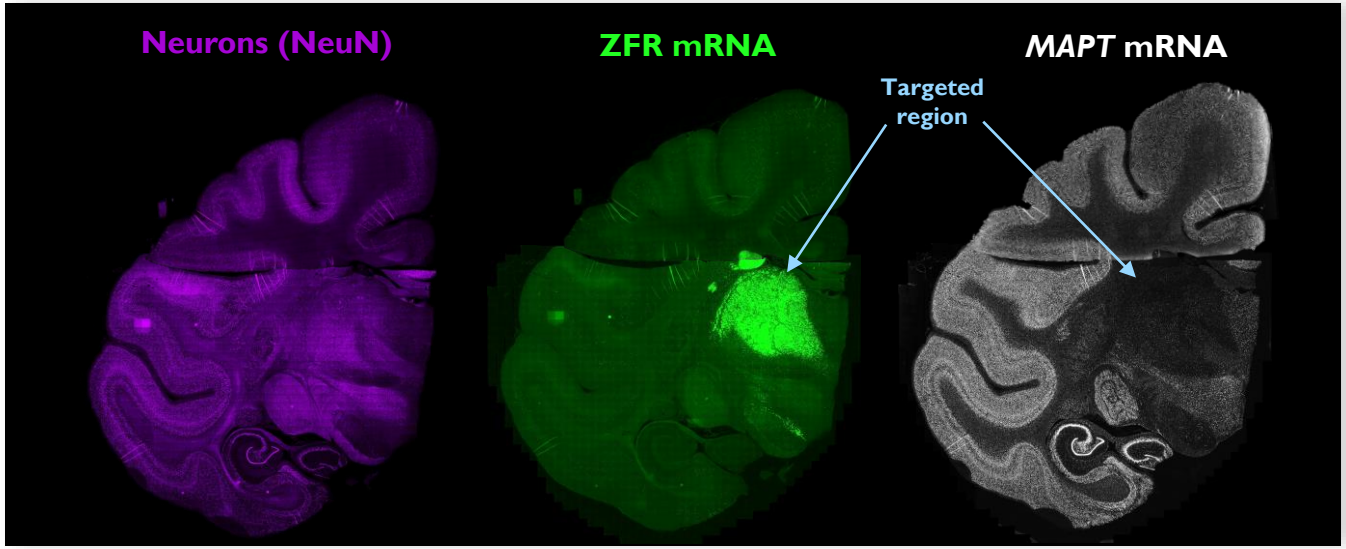
- Putamen
- Globus pallidus
- Thalamus



AAV9



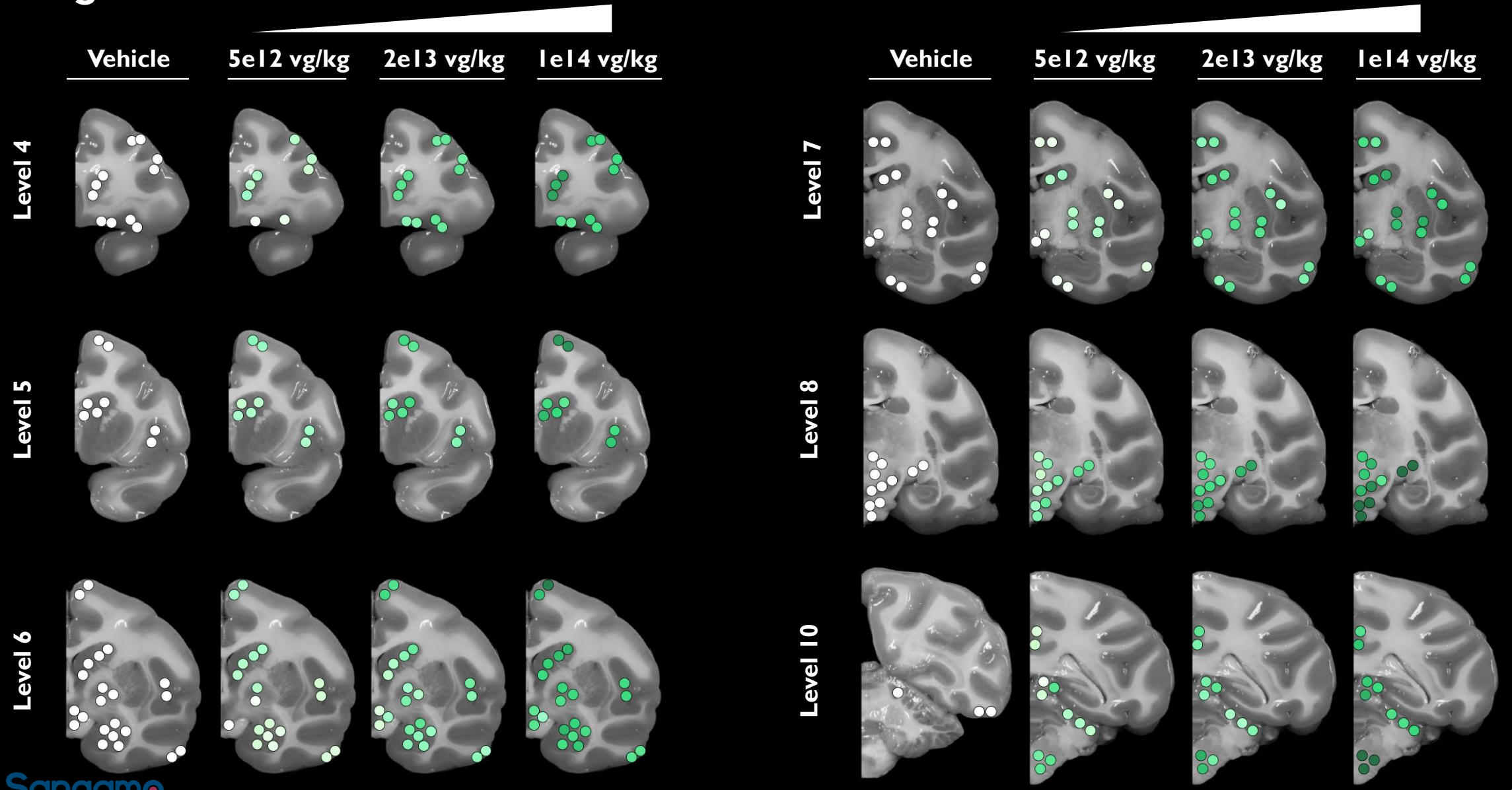
Axial view post infusion with gadolinium tracer



Multiplexed RNAscope ISH / IHC assay conducted on three brain levels, n=4 sections per level, per animal

MAPT = gene that encodes tau.

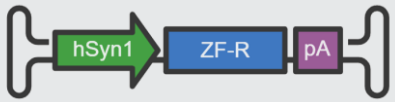
STAC-BBB mediates a clear dose response curve for tau ZFR expression throughout NHP brain



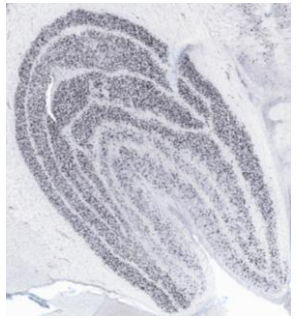
One NHP from each dose group shown, 28 days post administration, RT-qPCR bulk analysis

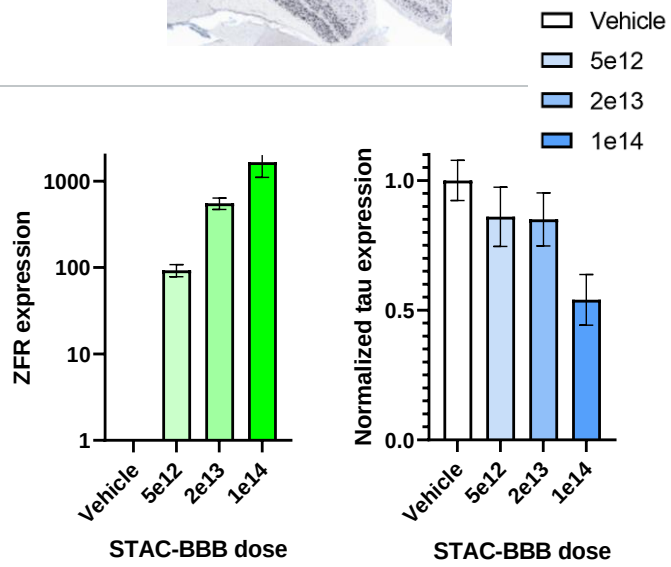
ZFR expression results in dose-dependent tau mRNA repression in bulk analysis of key brain regions

- Mean expression levels show a dose response for ZFR expression and tau mRNA repression in neurons
  - Bulk analysis includes all cell types and all punches for that region
- Neuronal tau is key to disease progression in tauopathies
- Tau ZFR is expressed only in neurons (Synapsin promoter)

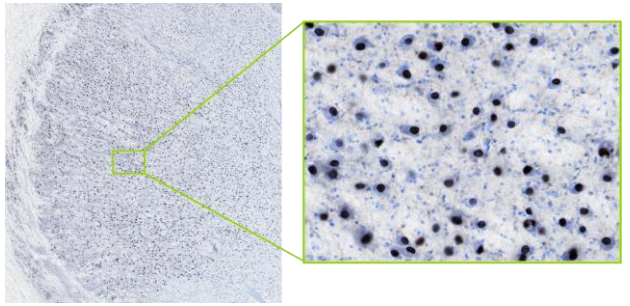


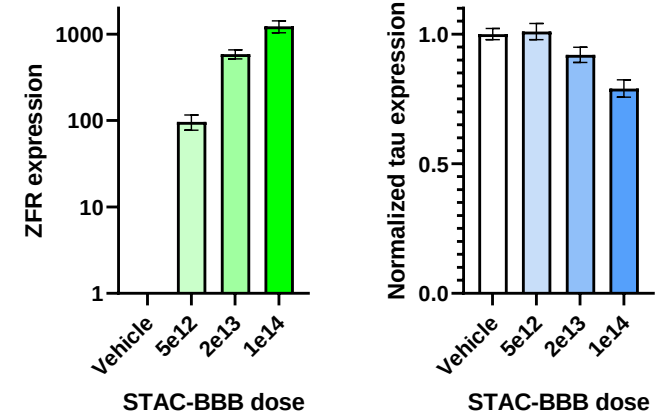
Lateral geniculate nucleus





Thalamus



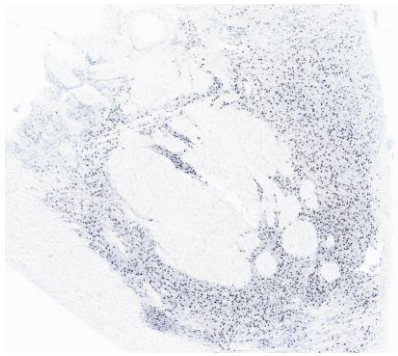


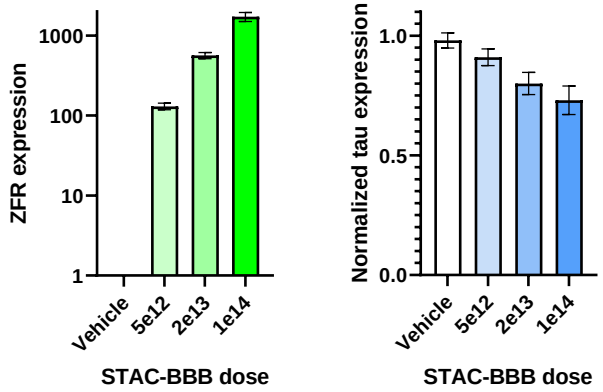
Chromogenic IHC images from reporter arm

Bulk analysis of brain punches, normalized to vehicle

STAC-BBB mediated bulk tau repression translates to potent neuronal suppression at the single cell level

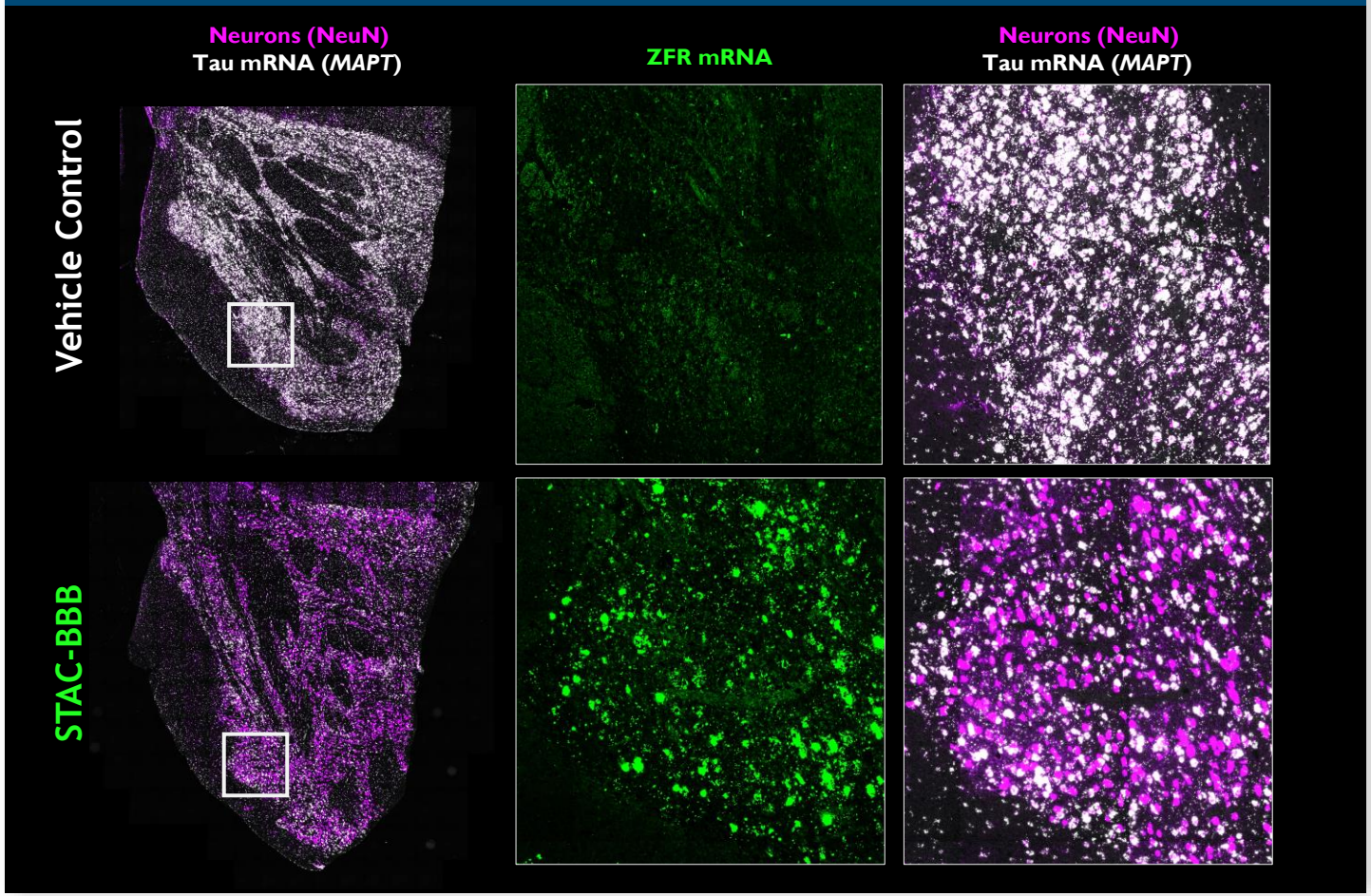
Pons: Bulk ZFR and tau mRNA





Chromogenic IHC image from reporter arm
Bulk analysis of brain punches, normalized to vehicle

Pons: Single-cell ZFR and tau mRNA



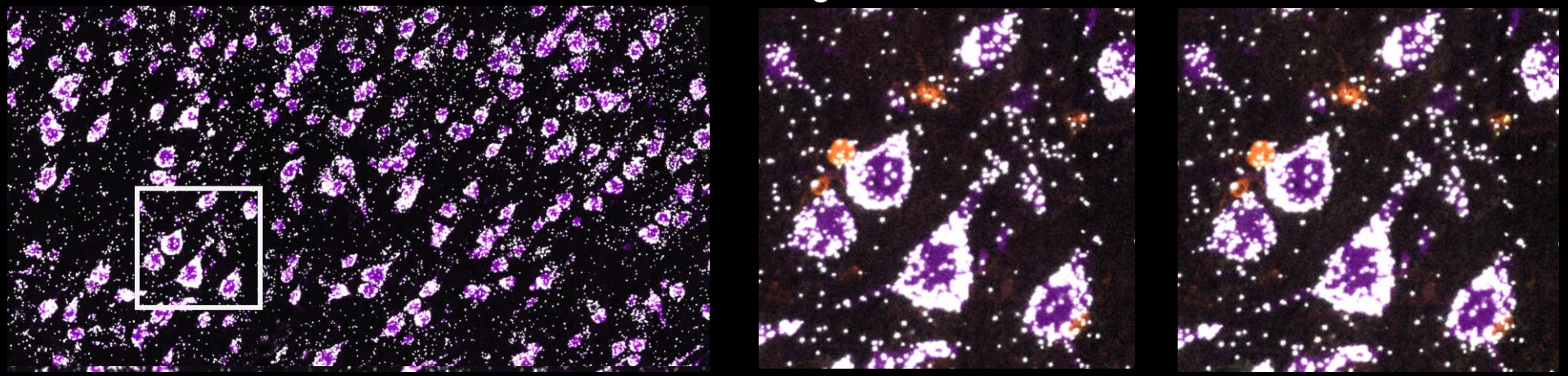
Multiplexed RNAscope ISH / IHC assay for NeuN, MAPT mRNA, and ZFR mRNA
1e14 vg/kg dose, 28 days post administration

Sangamo THERAPEUTICS

Single cell analysis also shows potent and selective repression of neuronal tau in the motor cortex

In control animals, tau mRNA is detected in neurons and glia. No ZFR is detected.

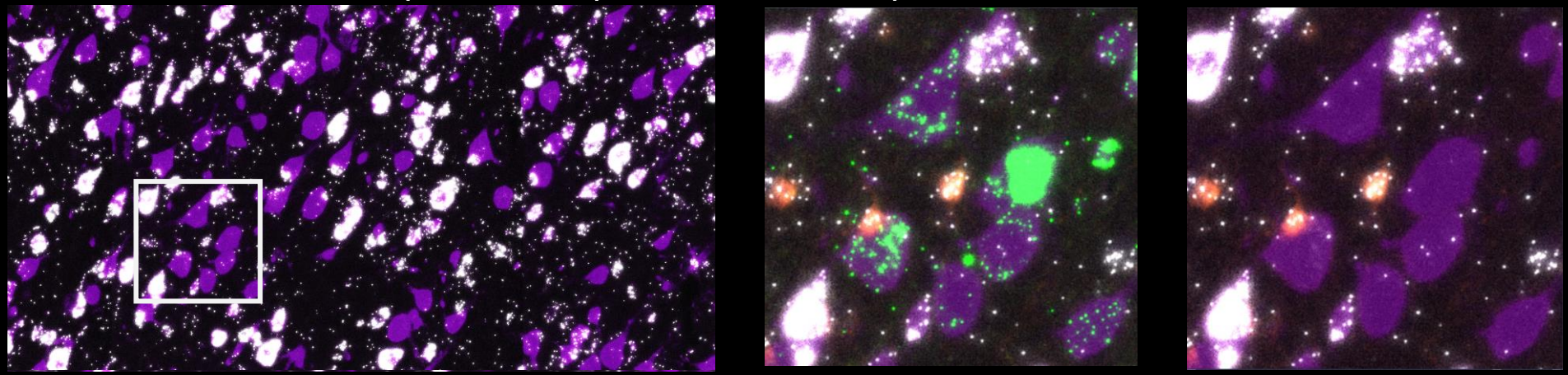
Vehicle Control



Glia (S100β)
ZFR mRNA
Neurons (NeuN)
Tau mRNA (MAPT)

STAC-BBB mediates ZFR expression and potent tau mRNA repression in neurons

STAC-BBB



Multiplexed RNAscope ISH / IHC assay for NeuN, S100β, MAPT mRNA, and ZFR mRNA
1e14 vg/kg dose, 28 days post administration

Sangamo THERAPEUTICS

Sangamo's tau program is well advanced and ideally placed for a potential partner to advance into clinical studies

Summary

- Clinical lead ZFR with >95% tau reduction per cell, no off-targets, and exceptional potency *in vitro* and *in vivo*
- Target engagement, efficacy, durability, and safety in two mouse models – APP/PS1 and htau
- Evaluated multiple capsids and routes of administration in NHP confirming pharmacology and safety; IV route favored with STAC-BBB capsid
- We expect the IND submission could occur as early as the fourth quarter of 2025*.

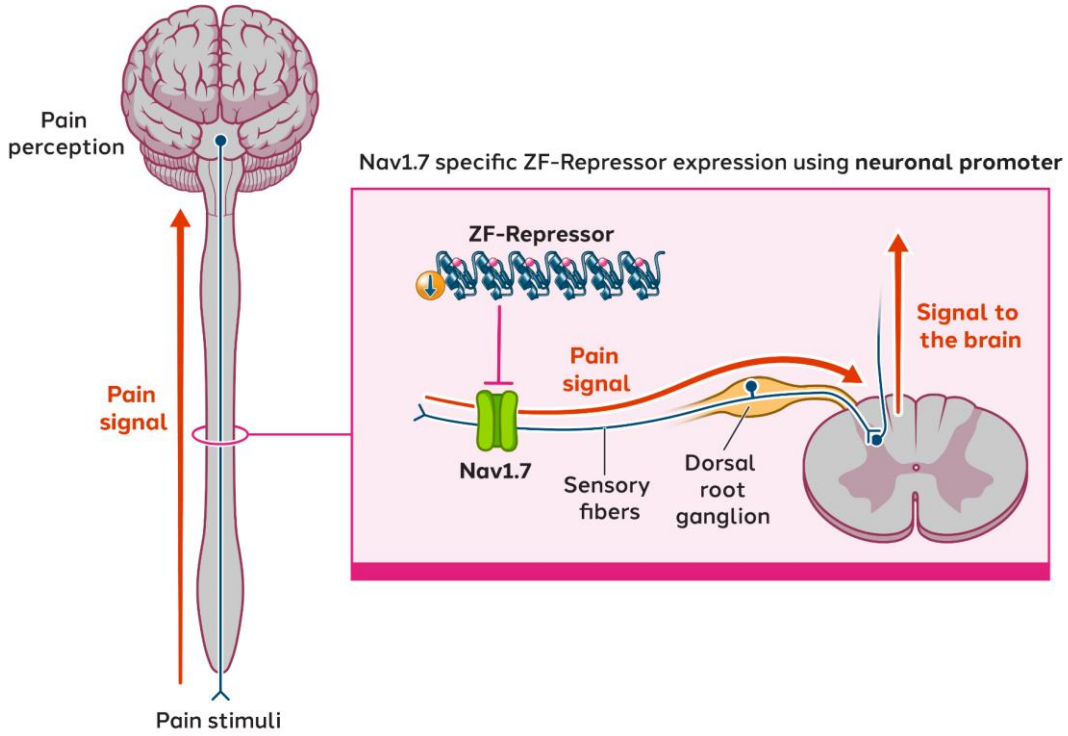
Activity, Status	 ZFR design, screening	In vitro validation	Rodent TE, safety	Rodent efficacy	NHP dose, TE, safety	NHP GLP/TOX	**IND Q4 2025***
Models	Human cell line Mouse cell line Human fibroblasts	Human iPSC neurons Mouse neurons	Wildtype mice htau mice	APP/PS1 mice htau mice	Cynomolgus NHP, Multiple ROAs and capsids evaluated	Could be initiated as early as Q2-2024	
Endpoints	*MAPT* mRNA Transcriptomics	*MAPT* mRNA Transcriptomics Tau protein	*MAPT* mRNA Transcriptomics Tau protein Single-cell ISH/IHC Safety/pathology	ptau pathology Dystrophic neurites *MAPT* mRNA Tau protein Single-cell ISH/IHC Safety/pathology	*MAPT*, ZFR mRNA Single-cell ISH/IHC Biodistribution Tau protein Safety/pathology		

** Subject to our ability to secure adequate funding*

Balancing Risk Through a Diversified Delivery Approach

Urgent need for novel chronic neuropathic pain therapeutics

Leverages an AAV delivery capsid already in the clinic. Targets a gene validated by human genetics. Targets a patient population with high unmet medical need. Gateway to additional indications.



- Nav1.7 is a voltage gated sodium channel expressed in the Dorsal Root Ganglion (DRG)
- Alterations in Nav1.7 activity **directly regulate pain levels** in several genetic disorders
- Blocking Nav1.7 in the DRG is expected to prevent the **transmission of nociceptive pain signals** to the brain
- This allows us to target multiple **neuropathic pain indications**, regardless of the cause of the pain
- Reducing pain by inhibiting Nav1.7 is not predicted to be associated with **any neurological side effects**

Zinc finger repressors potently reduce Nav1.7 in human neurons with exquisite and maximal specificity

iPSC-derived neurons

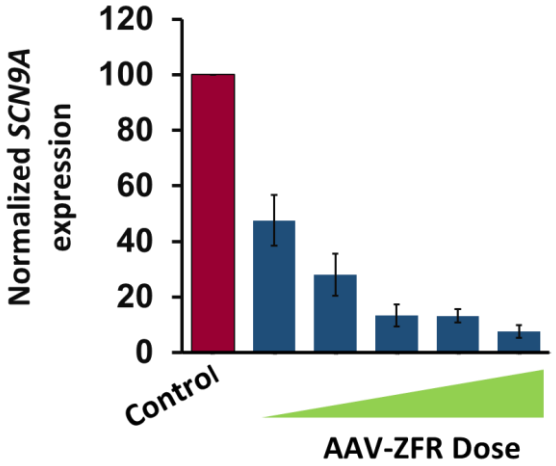
+

AAV + ZFR

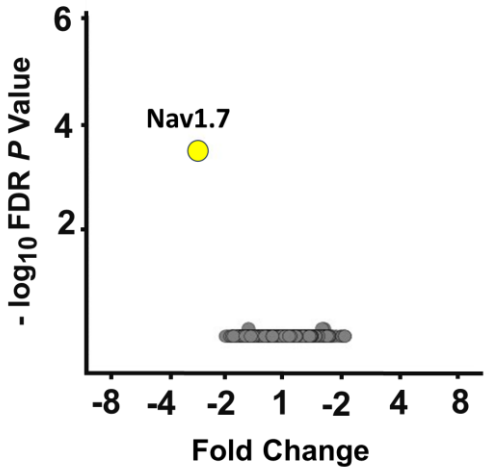
↓ 30d

Nav1.7 expression,
Off-target assessment

Potent and dose-dependent repression of *SCN9A* gene, which encodes Nav1.7

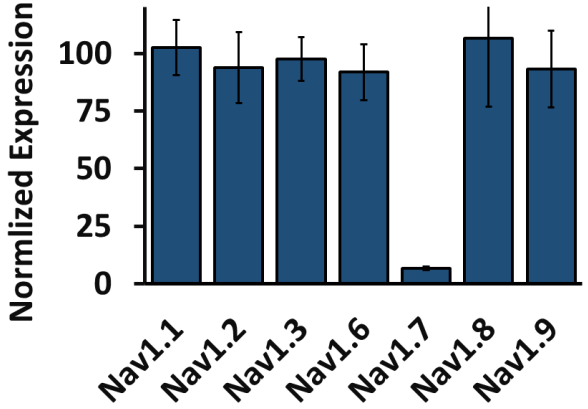


Selective repression of *SNC9A* as shown by global genomic analysis



Differential expression of 20,000 genes was evaluated

Specific repression of Nav1.7 without impacting other sodium channels

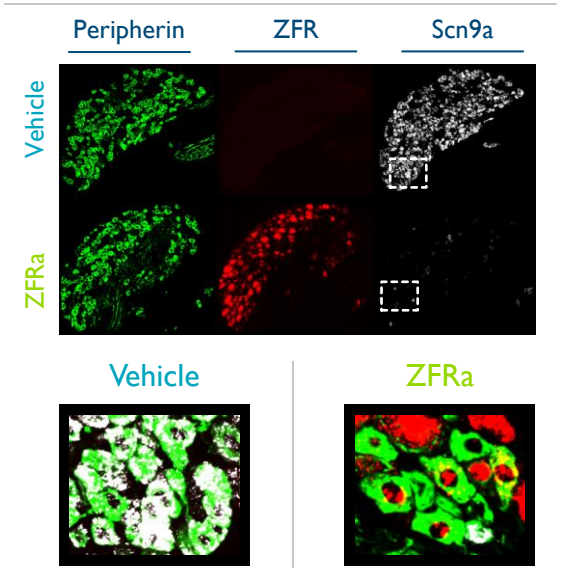


Nav1.7 repressors reverse neuropathic pain in preclinical models

IND-enabling GLP Toxicology studies are nearing completion. IND submission expected Q4 2024.

Potent Scn9a mRNA repression in mouse DRG neurons

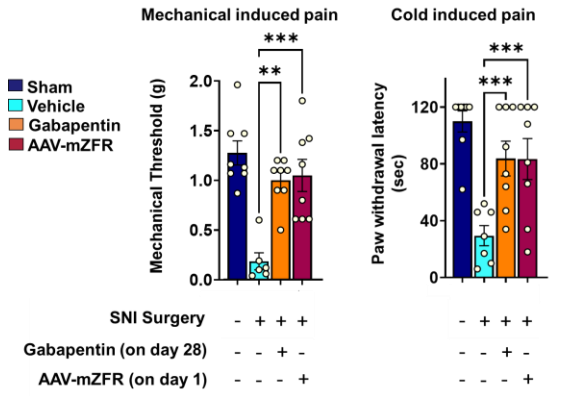
Intrathecal injection, **4 weeks**



Full restoration of mechanical and cold induced pain responses in mZFR-treated mice

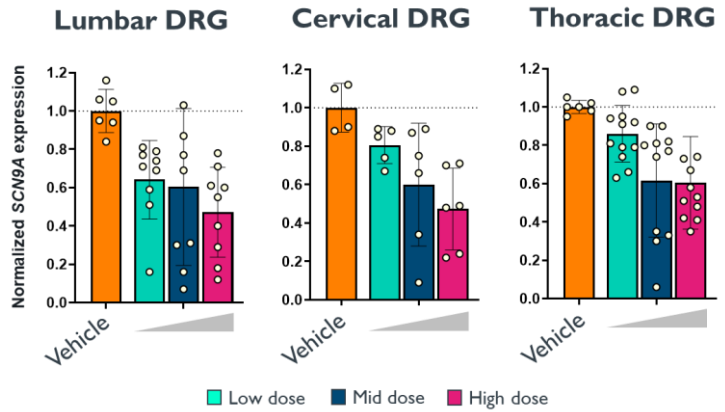
Intrathecal injection

Mechanical pain measurement



hZFR repressed SCN9A by up to 40-60% at the bulk tissue level across a 100-fold dose range

AAV/ZFRs
IT Injection



- Well tolerated across a 100x dose range
- No clinical signs of toxicity or clinical pathology findings
- No adverse macroscopic findings; minimal-mild DRG findings, not considered dose-limiting

Preclinical data from ASGCT 2023

Gabapentin was administered one hour before measurement
***p<0.01, ***p<0.001 vs Vehicle group*

The Nav1.7 program is in final toxicology studies, with an IND submission expected in 2024

Summary

- Clinical lead ZFR with >95% Nav1.7 reduction per cell, no off-targets, and exceptional potency *in vitro* and *in vivo*
- Target engagement, efficacy, durability, and safety and rescue of pain hypersensitivity in a mouse model of neuropathic pain
- Clinical candidate ZFR repressed Nav1.7 mRNA by up to 40-60% at the bulk DRG level across a 100-fold dose range in the NHPs
- Clinical lead ZFR was well tolerated at all doses tested and not associated with any in-life clinical or neurological observations, with minimal adverse microscopic findings
- 3-month GLP toxicology study is complete, with 6-month time point to be completed in Q1 2024. IND submission expected Q4 2024*.

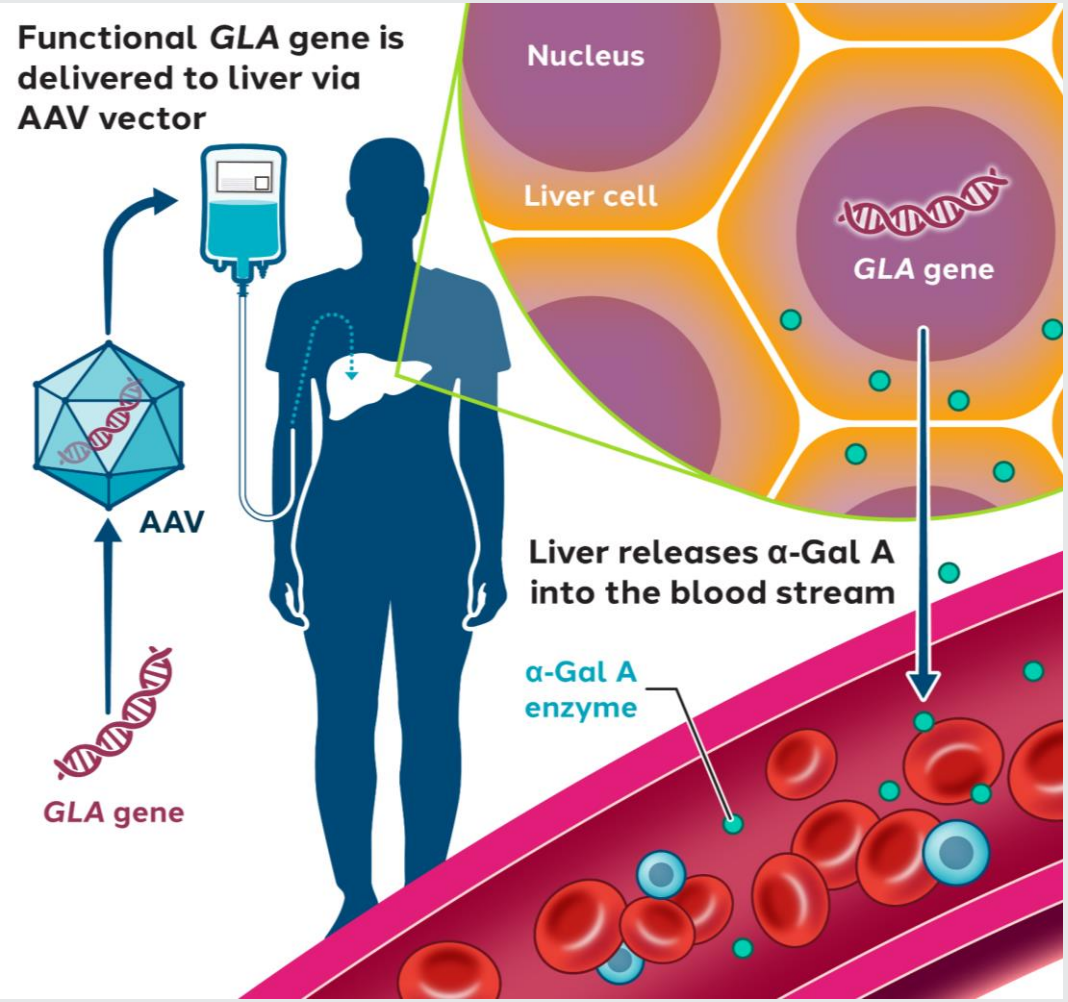
Activity, Status	 ZFR design, screening	 In vitro validation	 Rodent TE, safety	 Rodent efficacy	 NHP dose, TE, safety	 NHP GLP/TOX	**IND Q4 2024***
Models	Human cell line Mouse cell line	Human iPSC neurons Mouse neurons	Wildtype mice	SNI pain model - 4 weeks post dosing	1-month Cynomolgus NHP	3- and 6- month Cynomolgus NHP	
Endpoints	Nav1.7 mRNA Transcriptomics	• Nav1.7, ZFR, and other Nav channel mRNA • Transcriptomics • Nav1.7 function	• Nav1.7 mRNA Transcriptomics • Tolerability	• Mechanical and cold induced pain • Nav1.7, ZFR mRNA • Single-cell ISH/IHC • Safety and behavior	• Nav1.7, ZFR and other Nav mRNA • Single-cell ISH/IHC • Biodistribution • Immunogenicity • Safety/pathology	• Nav1.7, ZFR mRNA • Biodistribution • Toxicokinetics • Immunogenicity • Safety/pathology	

** Subject to our ability to secure adequate funding*

Optimizing Value of Clinical Programs

Fabry Disease: isaralgagene civaparvovec (ST-920)

Abbreviated clinical pathway supports efforts to secure a collaboration partner



- Largest gene therapy program in Fabry disease
  - 32 patients dosed in Ph1/2 STAAR study
  - Expect to complete dosing of remaining enrolled patients in 1H24
- Compelling clinical data
  - Sustained, elevated α-Gal expression up to 3 years
  - 13 patients off Enzyme Replacement Therapy (ERT)
  - Improvements in disease severity, quality of life and gastrointestinal symptoms
- FDA alignment on abbreviated regulatory pathway
  - Aligned on a single-arm study with up to 25 patients, alongside confirmatory evidence, as an acceptable pathway to BLA
- Received EMA PRIME eligibility
- Received UK MHRA ILAP status

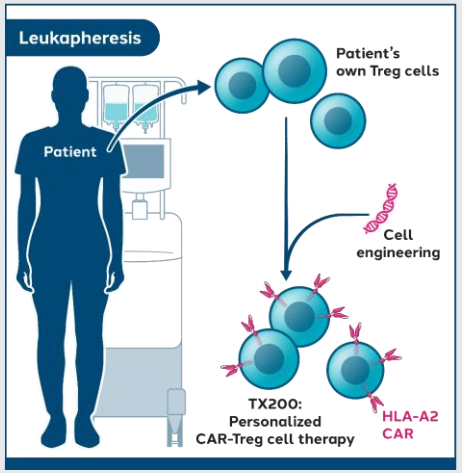
Fabry Disease: isaralgagene civaparvovec (ST-920)
Summary of updated Phase 1/2 STAAR study data, as presented at WORLD*Symposium* 2024

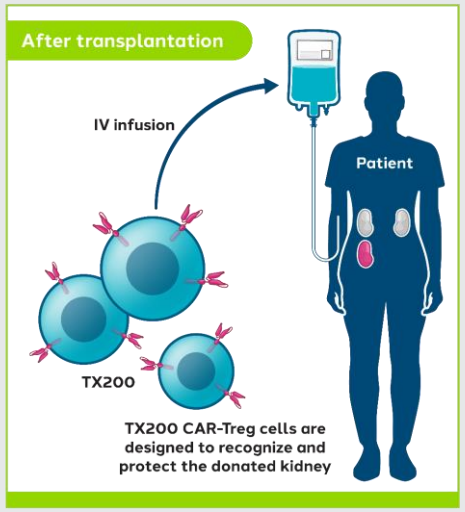
- ST-920 gene therapy was well-tolerated with an excellent safety profile in this population of adults with symptomatic Fabry disease:
  - No prophylactic steroids/other immunomodulatory agents administered
  - No LFT elevations requiring steroids
- Durable efficacy was demonstrated, with supraphysiological levels of α-Gal A activity maintained for up to 36.2 months
  - Largest plasma lyso-Gb3 reductions seen in naïve/pseudo-naive subjects with highest baseline values
- Compared to baseline, the 13 subjects with ≥12 months of follow-up showed:
  - Renal function remained stable
  - Significant improvement in FOS-MSSI disease severity score, with 38% of subjects on ERT improving in disease severity category
  - Significant improvement in SF-36 QoL and GSRS GI symptom scores
- All 12 subjects who discontinued ERT have remained off ERT for up to 19 months, as of the data cut-off
  - 11/12 have maintained sustained supraphysiological α-Gal A activity (1 with sustained α-Gal A activity in normal physiologic range)
  - 75% (6/8) had an improved disease severity score at 12 months compared to their baseline severity score on ERT
- Total or neutralizing α-Gal A antibodies decreased markedly in 7 subjects and became undetectable in 5 (71%)
- ***ST-920 has potential as a one-time, durable treatment option for Fabry disease that can improve patient outcomes***

Clinical data from WORLD, February 2024

CAR-Treg cell therapy

Seeking collaboration partner or direct investment

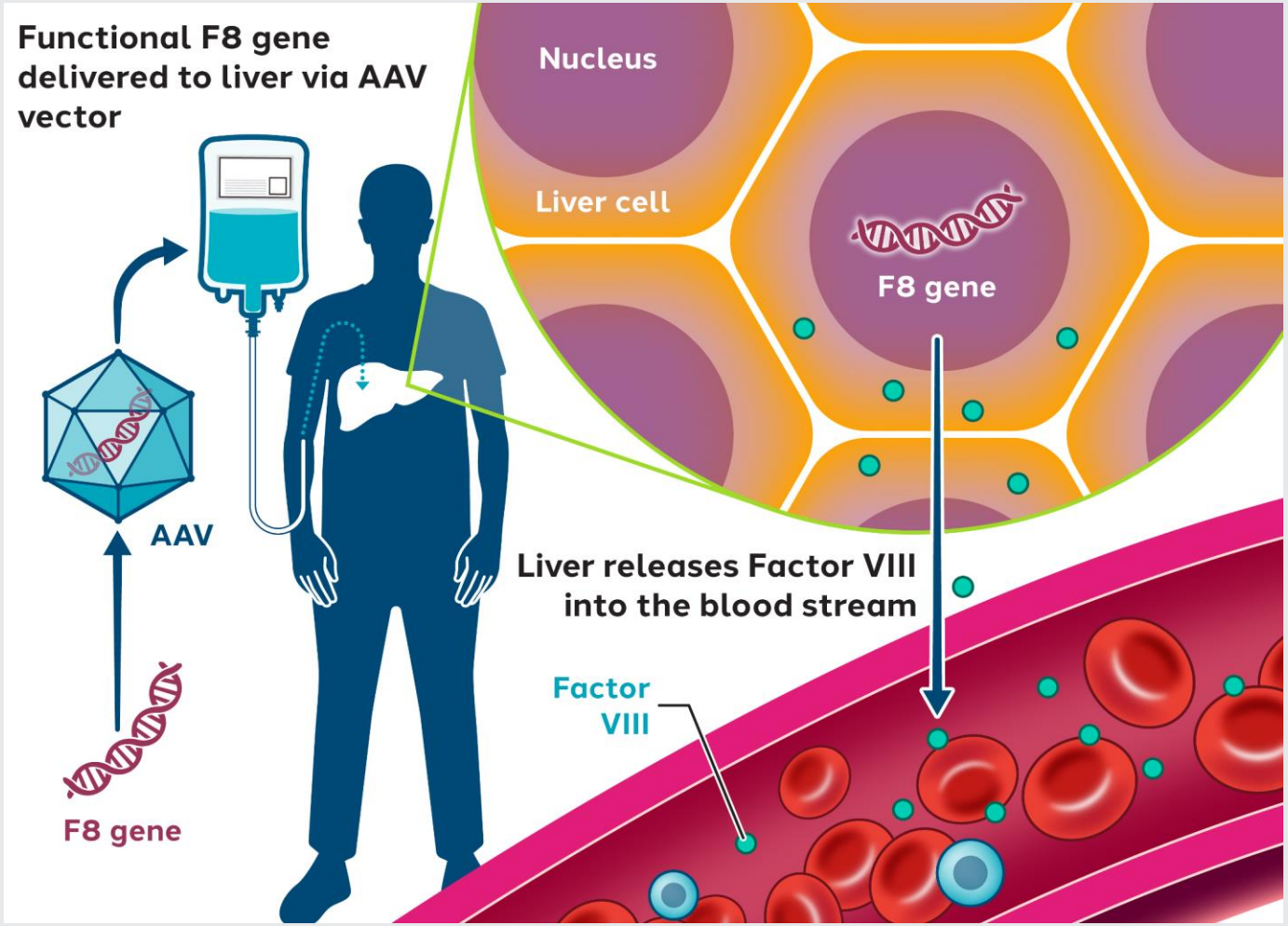




- Six patients dosed in Phase 1/2 STEADFAST study of TX200 for the prevention of immune mediated rejection in HLA A2 mismatched kidney transplantation, including the first patient in the new highest dose cohort
- The product candidate continues to be generally well tolerated in all patients dosed to date
- In alignment with previously announced strategic transformation, announced winddown of the Company's French research and manufacturing operations and a corresponding reduction in workforce
- Plan to complete dosing in the Phase 1/2 STEADFAST study and to continue seeking a potential collaboration partner or external investment in the autologous CAR-Treg cell therapy programs

Hemophilia A: giroctocogene fitelparvovec (Pfizer)

Progressing toward pivotal readout for Phase 3 AFFINE trial



- Program transitioned to Pfizer for Phase 3 development
- Dosing in Phase 3 AFFINE trial is complete
- Pivotal readout expected mid-2024
- BLA and MAA submissions anticipated early 2025
- Potential to generate up to **$220 million in remaining milestone** payments*, and **14-20% royalties on future product sales** if approved**

*beginning in 2025. **subject to customary reductions

Sangamo is a differentiated genomic medicine company focused on treating debilitating neurological diseases

Sangamo THERAPEUTICS

Potent zinc finger epigenetic regulation technology, with neurology programs advancing towards the clinic

Industry-leading AAV capsid discovery platform enabling non-invasive intrathecal and intravenous delivery to the brain

Powerful research platform **continually innovates in new modes of genome modulation** to support value creation for both wholly owned programs and potential partners

SHARP STRATEGIC FOCUS IN NEUROLOGY

Track record of successful partnerships, with $220m in potential near-term milestones from Pfizer (Hem A BLA submission expected early 2025). **Seeking partner for Fabry program, with clear pathway to potential registration.**

OPTIMIZING ASSET VALUE